VOL. CLXVIII, No. 3 SEPTEMBER, 1924 No. 630

THE

AMERICAN JOURNAL OF THE MEDICAL SCIENCES

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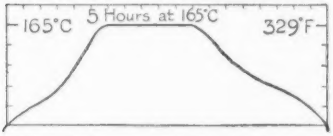

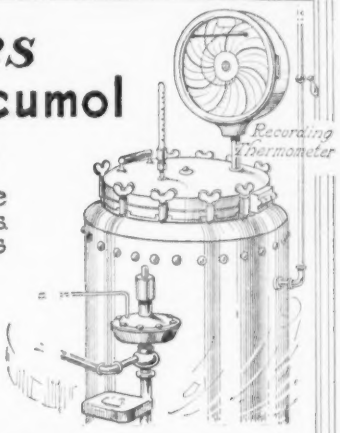

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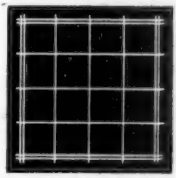
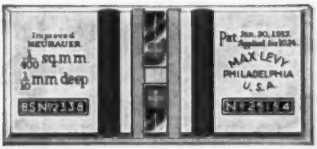


FIG. 1

Group of 16 smallest squares of **Improved** Neubauer ruling showing split boundary lines



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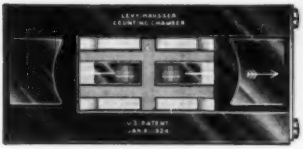

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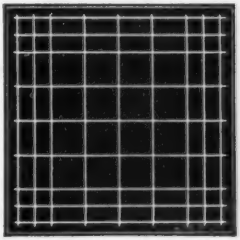

FIG. 2

Group of 16 smallest squares of **original** Neubauer ruling showing boundary by fifth squares with extra line in middle of each.

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In the Thoma and in the original Neubauer rulings this was accomplished by an extra line in the middle of every fifth square. (See **Fig. 2.**)

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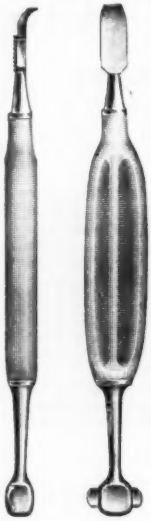

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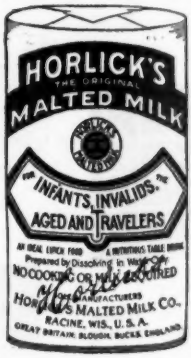

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Leaves from a DIGITALIS NOTE BOOK

No. XI

By. F. A. Upsher Smith, Ph. C.

PUBLISHED REPORTS

(CONTINUED)

DR. E. L. TUOHY, of the Duluth Clinic, in a paper on "Mitral Stenosis," gives the following case report:—

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"Mrs. H. A. G., aged thirty-nine (No. 19140). Rheumatic fever when sixteen. First signs of cardiac failure after second baby eight years ago—very rapid heart in fibrillation, extreme exhaustion, much dyspnea (particularly on lying down), chest pains on slight exertion, much gas and bloating (attributed to her food).

"Patient anxious, alert, pallid, thin, lips slightly cyanotic. Tachypnea; throbbing of the vessels of the neck; wide, diffuse apex beat; suggestion of a presystolic thrill. Liver edge markedly rounded and tender. Slight edema of the ankles.

"Fluoroscope showed definite widening, both to the right and to the left, and distinct enlargement of the left auricular shadow. Blood pressure, 80 diastolic and 130 systolic. Hemoglobin, 80 per cent; red blood cells, 4,900,000; white blood cells, 10,000. Urine showed albumin; no blood and no casts.

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MANUAL OF SURGICAL ANATOMY

By

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Dean, College of Medicine, University of Illinois; Professor and Head of Department of Anatomy, Histology and Embryology

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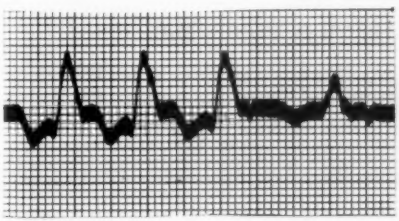

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Smallpox
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Photo, courtesy Michigan Department of Health, 1924

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The disease may assume a highly virulent and hemorrhagic form at any time, as witness the case here pictured, which occurred in Michigan as recently as June, 1924.

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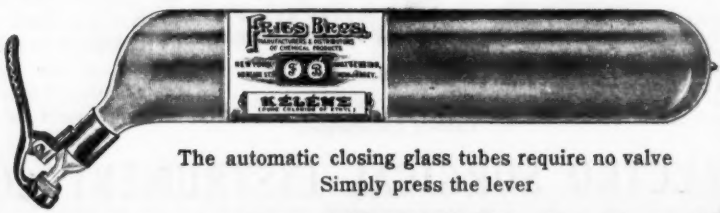

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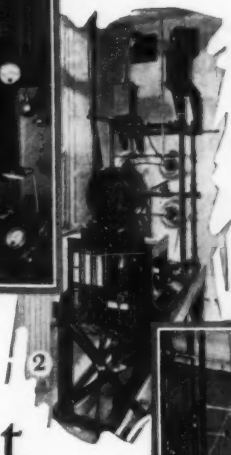

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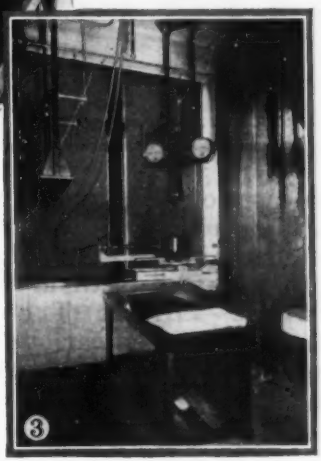

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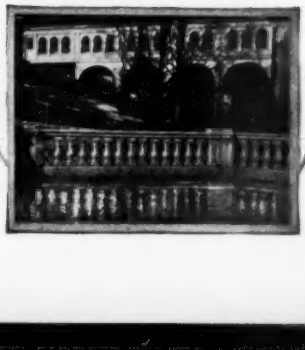

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OF THE MEDICAL SCIENCES

SEPTEMBER, 1924

ORIGINAL ARTICLES.

THE CAUSE OF DEATH IN DIABETES MELLITUS.

By Reginald Fitz, M.D.,

and

Wm. P. Murphy, M.D.,

Boston, Mass.

(From the Medical Clinic of the Peter Bent Brigham Hospital.)

Introduction. Insulin will probably change the clinical picture and course of diabetes to a very considerable extent. In order to contrast what may happen in the future with what has happened in the past, it is important to put on record all possible cases completely studied before insulin came into general use. With this idea in mind we have analyzed the records of all the cases of diabetes in the Peter Bent Brigham Hospital which have died in the hospital after entering the medical wards.

We have divided the cases into two groups. The first group contains those cases dying in the hospital before January 1, 1923 and the second comprises those cases dying during 1923. We have made this arbitrary division because we have become fairly familiar with the use of insulin during 1923 and thus have a year's experience with the new remedy to contrast with almost ten years' experience without it.

Diabetes from 1913 to 1923. From 1913, when the hospital first opened until January 1, 1923, the diagnosis of diabetes mellitus was made in 562 cases admitted to the medical wards. Of these, 64 died in the hospital.

One interesting fact brought out from study of the records is

that the mortality was not constant from year to year but showed a surprising variability. In order to make this clear, the number of new cases admitted each year was tabulated and the number of deaths occurring among them. The data is given in Table I.

TABLE I.—THE VARIABILITY OF DIABETIC MORTALITY.

Year.	New cases admitted.	New cases dying in hospital.	Mortality per 100 cases.
1913 and 1914	46	2	4
1915	60	7	12
1916	72	9	12
1917	70	4	6
1918	57	7	12
1919	47	3	6
1920	60	1	2
1921	64	6	9
1922	86	10	12
Total	562	49	9

The annual mortality for the new cases varied between 2 and 12 per cent with an average mortality of 9 per cent. It is important to bear in mind that such variability in the mortality of new diabetic cases treated in a general hospital from year to year is possible. The explanation probably lies in the fact that diabetes may be either a very mild or a severe form of disease. Any form of hospital treatment will appear to be accompanied by a low immediate mortality if a sufficient number of mild cases are treated. On the other hand, a small sequence of severe cases will exaggerate the inevitable mortality which accompanies any chronic disease requiring hospital care. On the whole, therefore, conclusions in regard to the value of treatment as it affects the hospital mortality of diabetes may be of dubious value.

Of the 64 fatal cases, 55 were able to date the onset of their disease with a fair degree of accuracy. Thus we estimated the duration of diabetes in these cases, arranging the results according to age at the time of death. The results are shown in Table II.

TABLE II.—THE DURATION OF DIABETES.

Age at death.	Total number of cases.	Total duration of diabetic life, years.	Average duration of diabetic life, years.	Shortest duration of diabetic life, years.	Longest duration of diabetic life, years.
61 to 80	12	97.7	8.1	0.1	16
51 to 60	12	68.2	5.7	0.2	15
41 to 50	10	37.5	3.7	0.1	8
21 to 40	14	15.3	1.1	0.1	4
Less than 21	7	6.3	0.9	0.1	2
Total series	55	225.0	4.1		

This table shows, strikingly, the well-known fact that diabetes tends to become less severe as the age at which symptoms are first

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19 Jy 44

recognized becomes greater. On the other hand, it illustrates the fact that acute diabetes may develop in persons of almost any age so that increasing years do not necessarily preclude a severe form of the disease.

Of the 64 fatal cases, 58 (90 per cent), entered the hospital shortly before death and had not been treated previously as Peter Bent Brigham Hospital patients. On the other hand 8 of the fatal cases in this series were able to date the onset of their diabetic symptoms and were treated by the hospital at more than one entry for varying lengths of time before death. It is interesting to see how the effect of hospital instruction and subsequent follow-up care manifested itself in the duration of these patients' lives. The data is shown in Table III.

TABLE III.—THE EFFECT OF TREATMENT ON THE DURATION OF DIABETIC LIFE.

Peter Bent Brigham medical number.	Age at death.	Duration of diabetic symptoms before treatment, years.	Duration of life after treatment, years.	Total duration of diabetes, years.	Average duration of diabetic life for patient of same age (taken from Table II.) years.
20064	64	6.0	1.8	7.8	8.1
6792	59	3.0	2.2	5.2	5.7
16376	52	0.3	7.7	8.0	5.7
6343	49	0.7	3.4	4.1	3.7
15067	48	1.0	7.5	8.5	3.7
14721	27	0.2	3.6	3.8	1.1
13363	19	0.1	1.1	1.2	0.9
16886	13	0.7	0.8	1.5	0.9

All but 2 of the cases treated for any length of time by the Peter Bent Brigham Hospital had a longer diabetic life than the average case of comparable age which entered the hospital just before death. Thus the treatment given appeared of definite value in prolonging life.

Physicians who treat many diabetics recognize the importance of early treatment in the course of any given case and realize that the best therapeutic results by any method are usually obtained in those cases which are thoroughly treated as soon as possible after the onset of illness. The justification for this belief is well shown by Peter Bent Brigham Hospital Medical No. 14721 who entered the hospital on April 16, 1917. The patient was a young woman, aged twenty-three years, who developed diabetic symptoms two months before entry. She was followed by the Hospital Staff until her death nearly four years later, and during this interval re-entered the hospital several times. At each entry certain details of treatment were changed. From the records, however, we were able to estimate from Woodyatt's formula the total glucose tolerance attained at each entry, and thus have a fairly accurate picture of the course of the disease. The case is of particular value as a necropsy was performed, showing no gross anatomical changes except calcifi-

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cation of the mesenteric lymph nodes. The essential findings to illustrate the course of the disease in this case are given in Table IV.

TABLE IV.—THE COURSE OF AN UNCOMPLICATED CASE OF DIABETES.

(Peter Bent Brigham Medical No. 14721. A woman 23 years old. Diabetic symptoms of two months' duration.)

Date.	Weight, kg.	Systolic blood pressure.	Glucose tolerance, gm.	Comment.
April 16, 1917 . . .	51.2	130	129	
Sept. 10, 1918 . . .	46.0	120	152	
Oct. 8, 1919 . . .	48.0	125	199	Before this entry patient gave up her diabetic diet.
Mar. 12, 1920 . . .	42.6	107	131	Before this entry patient gave up her diabetic diet and had an acute respiratory infection.
Nov. 4, 1920 . . .	39.0	104	...	Before this entry patient gave up her diabetic diet. Death in coma.

For almost two years and a half there was but little loss of weight, no fall in blood-pressure and an apparent gain in tolerance. After this experience with diabetic dieting the patient apparently became discouraged although she appeared to be doing well, and gave up taking care of herself. Then there followed a precipitous loss of weight, fall in blood-pressure, fall in tolerance and final death in coma.

Such an initial two-and-a-half-year record in a case treated shortly after the onset of symptoms is not unusual even in the youngest people. One must remember this fact in discussing the effect on tolerance of any specific form of treatment. For instance, it is reasonable to assume that in this particular case any restricted calory diet with a gram or less of protein per kilogram of body weight, whether it contained a high carbohydrate low-fat mixture or a low carbohydrate high-fat mixture would have been followed by an apparently increased tolerance and symptomatic improvement if given to the patient at any time during the first two and a half years of her diabetic life. This case serves as an example to illustrate how careful one must be in drawing conclusions, especially with insulin, in regard to the effect of treatment on tolerance. Cases will have to be studied for a long time in a most critical fashion before any accurate knowledge on the matter can be obtained.

Of the 64 fatal cases in the entire series, 37 were examined pathologically and thus the true cause of death is known. There were 4 coma cases (11 per cent) which showed no particular gross anatomical changes and in which the patients appeared to die from what may be called uncomplicated diabetic coma. There were 14 cases (38 per cent) which, with or without coma, had an obvious sepsis or a terminating acute infection. There were 7 cases of active pulmonary tuberculosis (19 per cent). There were 3 cases (8 per

cent) with unusual complications such as hypernephroma in 1 case, hemachromatosis in 1 case and lymphatic leukemia in 1 case. There were 9 cases (24 per cent) with cardiovascular complications including gangrene or nephritis. In other words, uncomplicated diabetic coma was a rare cause of death, while coma combined with infection was common; active pulmonary tuberculosis caused nearly as many deaths as did cardiovascular disease. One interesting observation brought out from the analysis of the autopsied cases was that diabetic coma, on the whole, was the common cause of death in the young people; pulmonary tuberculosis also tended to be a cause of death in this group as it occurred in five instances in people under forty and only twice in older persons; sepsis or a terminating infection of any sort occurred in diabetics of all ages; the cardiovascular or renal complications and gangrene were reserved for the elderly patients.

Three other interesting points came up in this study: Anemia as judged by the red blood cell count was very rarely seen. Leukocytosis shortly before death was common. Syphilis, as revealed by a positive serum Wassermann test or by gross anatomical evidence, was unusual.

Red-blood counts were made in 33 cases, and in only 7 was the count below 4,000,000. One of these cases had septicemia, 1 had hemachromatosis, 2 had advanced chronic nephritis with a zero phthalein excretion, 1 had tuberculous bronchopneumonia, 1 developed anemia rapidly after an amputation of the leg for gangrene, and 1 was supposed to have cirrhosis of the liver and syphilis. In each instance, therefore, significant anemia was of definite prognostic significance and pointed to a serious complication.

White blood counts were made in 60 cases shortly before death. In 34 cases the white count was more than 16,000 and in only 10 cases was it less than 10,000. The white blood counts in the cases of severe acidosis are shown in Table V.

Of the 28 cases only 9 had a white blood count of less than 15,000 and only 3 of less than 10,000. Furthermore leukocytosis was often found in the absence of any demonstrable infection. It is thus apparent that leukocytosis tends to accompany severe diabetic acidosis. This fact may be of clinical significance. Leukocytosis may well be due to the concentrated blood so often found in diabetic acidosis due to anhydremia, or it may be due to infection without signs or symptoms which an acidotic diabetic patient acquires just before death. Therefore patients with acidosis must be given plenty of fluid and must be protected from exposure to infection in every possible way.

Blood Wassermann tests were made in 50 cases and were negative in 45. One case with a positive test was found at necropsy to have lobar pneumonia of the left lower lobe, general anasarca, chronic adhesive pleurisy of both lungs, chronic adhesive perihepatitis,

adhesive pericholecystitis, edema of the pancreas with connective-tissue increase and atrophy of the islands of Langerhans. A second necropsied case with a positive test was found to have suppuration of the ethmoidal cells and middle ear with acute meningitis, healed bilateral pulmonary tuberculosis and chronic fibrous pleuritis.

TABLE V.—THE WHITE BLOOD COUNT IN CASES OF SEVERE DIABETIC ACIDOSIS.

Peter Bent Brigham medical No.	White blood count.	Plasma bicarbonate or alveolar CO_2 in mm. of mercury.	Clinical cause of death.	Necropsy findings.
19254	20,800	20.2	Acidosis, septicemia	Generalized sepsis.
16732	4,900	10.2	Acidosis, arteriosclerosis	Arteriosclerosis. Acute pericarditis.
2862	4,600	19.0	Acidosis,	
19627	12,100	9.6	Acidosis, bronchopneumonia	Bronchopneumonia.
3907	19,200	8.9	Acidosis	
15067	14,500	....	Acidosis, chronic myocarditis	
7541	23,000	16.0	Acidosis	
16866	34,700	14.6	Acidosis, acute pericarditis	Acute pericarditis.
5798	31,600	....	Acidosis	
17049	16,300	13.3	Acidosis, pulmonary tuberculosis	Pulmonary tuberculosis.
6134	44,000	....	Acidosis	
15975	7,200	14.0	Acidosis	
2932	10,900	....	Acidosis	
20064	40,400	8.1	Acidosis, bronchopneumonia	Bronchopneumonia.
13271	13,000	17.1	Acidosis	Bronchopneumonia.
20128	26,000	....	Acidosis, sepsis	Bronchopneumonia, sepsis.
11330	10,800	14.0	Acidosis	
18002	21,250	....	Acidosis, bronchopneumonia	Bronchopneumonia.
14721	35,000	10.9	Acidosis	No infection demonstrable.
19653	14,300	....	Acidosis	No infection demonstrable.
12189	16,700	11.0	Acidosis	No infection demonstrable.
19183	13,600	....	Acidosis	
9979	41,800	10.0	Acidosis	
373	29,000	....	Acidosis	
9993	22,200	12.6	Acidosis, infection	
3283	18,000	20.0	Acidosis	Sepsis.
3224	44,800	12.7	Acidosis	No infection demonstrable.
3166	26,500	....	Acidosis	

The other cases with positive reactions were not autopsied. One apparently died of pneumonia, 1, a child of seven, in coma, and 1, following an amputation of the leg for gangrene, of arteriosclerosis with chronic myocarditis and heart failure. The large number of fatal cases with negative Wassermann reactions and without patho-

logical evidence of syphilis suggests that luetic diabetes is a very rare condition if it exists at all.

Taking the clinical records of the 64 fatal cases of diabetes as a whole there were 4 common causes of death. These causes were coma with or without a terminal infection, sepsis, cardiovascular or renal disease including gangrene, and pulmonary tuberculosis. Coma and pulmonary tuberculosis tended to occur in the younger patients, gangrene, cardiovascular or renal disease in the older patients, and sepsis in patients of any age. Additional facts of interest brought out in the review were that the annual mortality of new cases treated varied so much from year to year as to make conclusions with regard to the value of treatment as it affected the hospital mortality of diabetes during any one year of but little value. Diabetes became less severe as the age at which symptoms were recognized became greater although increasing years did not necessarily guarantee mild diabetes. Hospital treatment was of value in prolonging life. Coma, uncomplicated by a terminal infection, was rarely seen. Significant anemia was of prognostic significance as it pointed to a serious complication. Leukocytosis was the rule in severe acidosis. Syphilitic diabetes was a rare condition, if it existed at all.

Diabetes during 1923. During 1923, 124 new cases of diabetes were admitted to the medical wards of the hospital. Eight of these cases died, making the mortality for the year 6.5 per cent. In addition, 2 cases which had first entered the hospital previous to 1923 died, so that we have had 10 hospital deaths in all.

As has already been stated, the annual mortality of our new cases in the past has varied so much from year to year as to make conclusions in regard to the value of treatment as it affected the mortality during any one year of dubious value. Nevertheless it is interesting that the first year of insulin should have been accompanied by a mortality among the new cases appreciably lower than the average mortality during the ten previous years and only half as great as that of 1922.

Of the 8 fatal new diabetic cases in 1923, 4 were necropsied. The first patient, a girl, aged twenty-two years, died in typical coma. She had been receiving insulin for six weeks previous to her death and had been progressing satisfactorily until she became ill with a sore throat. Almost immediately glycosuria and acidosis developed. She was brought to the hospital in an ambulance from a city twelve miles away after being comatose for twelve hours and died shortly after entry. Necropsy showed a streptococcus septicemia.

The second patient was a man, aged fifty-two years, who also died in coma. His diabetic history was of about a year's duration although there had never been progressive loss of weight, polyuria or polydipsia. He was brought to the hospital after being unconscious for nearly twenty-four hours and he died shortly after admission. Necropsy was limited to an examination of the kidneys and

pancreas. These organs gave evidence of diabetes and a moderate degree of chronic nephritis.

The blood-sugar concentration at entry in this case was 0.84 per cent, the blood-urea nitrogen was 61 mg. per 100 cc of blood and the plasma CO_2 was 34.2 volumes per cent. The urine contained albumin, 5 per cent of sugar, and very little acetone or diacetic acid. The sediment contained rare leukocytes and occasional hyaline casts.

The case appears on our records as one of diabetes mellitus and diabetic acidosis. It is a question, however, whether the diagnosis of diabetic coma is justified in a case of diabetes not receiving alkali which dies comatose with no more marked a degree of acidosis than one producing an alkali reserve of 34 volumes per cent. The limited necropsy in this case did not help to clear up the diagnosis.

The third patient was a woman, eighty-five years of age. She had been under treatment for diabetes during the five years before her death and came to the hospital because of an acute respiratory infection. She died shortly after admission without evidence of acidosis. Necropsy showed that the chief cause of death was bilateral pneumonia. There was also a generalized arteriosclerosis.

The fourth case, a woman, aged fifty-two years, was known to have had diabetes for three years before her death. She had been feeling well until the day before admission when she suddenly became irrational, later drowsy and finally unconscious. Physical examination showed a marked degree of arteriosclerosis and a systolic blood-pressure of 200. No definite paralysis was noticed but the biceps and triceps reflexes were hyperactive on the left, there was spasticity of the left arm and a positive Babinski reflex on the left foot. The blood-sugar concentration was 0.32 per cent, the alkali reserve was 51 volumes per cent, and the blood-urea nitrogen was 22 mg. per 100 cc of blood. A single specimen of urine contained 2.8 per cent of sugar and a trace of albumin; the sediment contained numerous hyaline and finely granular casts. In view of the lack of acidosis and the presence of definite neurological signs the clinical diagnosis was made of diabetes mellitus, arteriosclerosis and intracranial hemorrhage. The patient died within a few hours. Necropsy showed generalized arteriosclerosis and marked coronary sclerosis. Permission to examine the head was not obtained.

Of the 4 fatal cases which were not necropsied 1, a woman, aged thirty years, died in coma after having had diabetic symptoms for a year. She became unconscious twenty-four hours before coming to the hospital and died a few minutes after entry. The second case was a woman, aged sixty-one years, who entered the hospital with a badly decompensated heart. She had no symptoms of diabetes but her urine contained 2.4 per cent of sugar and her blood-sugar concentration was 0.30 per cent. She died a few days after admission with signs of cardiac failure and with an alkali reserve of 46.2 volumes per cent. The third was a woman, aged seventy-six years,

known to have had diabetes for at least a year, and a carcinoma of the breast for a somewhat longer period. She entered the hospital with signs of a diffuse bronchopneumonia and died a few days later without any clinical manifestations of coma. The fourth case was a man, aged sixty-one years, who developed diabetic symptoms fourteen years previously and an intra-abdominal cancer about one year previously. He died about two weeks after entry without clinical manifestations of acidosis.

The two fatal cases of the 1923 series which entered the hospital for the first time previous to 1923, both died of heart failure. The first was a woman, aged sixty-two years, who entered the hospital in 1917, when, in addition to diabetes, she was found to have cardiac hypertrophy with dilation of the aortic arch and hypertension. There were no characteristic symptoms of diabetes, the glycosuria being found on routine analysis. After discharge she got along comfortably for five years when she became disturbed by increasing dyspnea and palpitation. She died a cardiac death without signs of acidosis although the urine contained sugar and the blood-sugar concentration was 0.32 per cent. Necropsy showed marked arteriosclerosis with hypertrophy and dilatation of the heart, and an aneurysm of the innominate artery.

The second case was a woman, aged sixty years, entering the hospital for diabetes in 1920. She was unable to date the onset of her illness with any accuracy, but was discharged in good condition on a liberal diet. She remained comfortable for two years when she suddenly experienced a severe cramping pain over the chest, neck and in both arms. On this account she made a second visit to the hospital, and in addition to diabetes was considered to have angina pectoris. Finally she entered for a third time in January, 1923, again having been comfortable until a recent sudden attack of precordial pain. She died a few days later without evidence of acidosis, the clinical cause of death being diabetes complicated by angina pectoris with a terminal infarct of the heart. Necropsy was not permitted.[1]

[1] Dr. Joslin has suggested that the hospitals of Boston establish the precedent of publishing all fatal cases of diabetes which occurred during the past year. In order to coöperate in this plan we are appending the 3 fatal diabetic cases which entered and died on the surgical wards of this hospital. The first was a woman, aged seventy-six years, with diabetes of eight years' duration. In addition she had physical signs of arteriosclerosis and myocarditis. She entered the hospital for a fractured hip and died without acidosis or coma, a few days later. The second case was a man, aged sixty-four years, who entered the hospital on March 21 with a gangrenous foot. Sugar was found in his urine; there was no diabetic history. On April 6 the patient had a mid-thigh amputation from which he made a normal recovery. On May 7 he developed erysipelas of the face from which he recovered. On May 26 (nine weeks after entry) he developed femoral phlebitis which was followed by death, June 1. The third case was a woman, aged sixty years, who entered the hospital with cholecystitis. There was no history of diabetes. A cholecystectomy and choledochostomy for cholelithiasis was performed under ether. After the operation the patient sank rapidly and died within twenty-four hours. A sample of urine obtained after the operation contained 2.6 per cent of sugar. The record does not make clear whether or not there was glycosuria before operation.

On the whole, then, during 1923 the causes of death in our diabetic patients have been much as in previous years: Our patients died of coma, sepsis, cardiovascular disease or its complications, and malignant disease. We have been fortunate in having no hospital deaths from tuberculosis.

Lessons to be Learned from Fatal Cases of Diabetes. Joslin has pointed out that there are always practical lessons to be learned from a study of fatal cases of diabetes. Our cases seem to us to give the following information: In the first place, the treatment of coma is of utmost importance; therefore a good understanding of this condition is essential. As has been shown from our records, diabetic coma is primarily a cause of death in young people; moreover almost all comatose diabetics have a complicating infection which may well play a part in causing death. In view of these facts it is extremely important to prevent the development of coma by proper supervision of cases, to make the diagnosis of coma as early as possible, and finally, if coma does develop, to safeguard the patient from infection in every possible way.

The prevention of coma is largely a matter of education. All diabetic patients, and especially young patients, must be taught to keep their urines sugar-free, to balance their diets so that acetone bodies are not formed and to recognize the possible significance of even very minor ailments. Moreover they must learn when to call upon a doctor, and that if they feel unaccountably ill, bed, an enema, plenty of water to drink and a diet of orange-juice and gruel are the routine orders until the doctor assumes the responsibility.

The diagnosis of coma is a medical problem. It is important to remember that it is not easy to make the diagnosis in every case, witness one of ours in which the diagnosis remains uncertain despite a careful physical examination, chemical studies of blood and urine and a pathological examination of the pancreas and kidneys. However, there are certain physical signs and symptoms which occur fairly constantly and which justify emphasis. Diabetic coma is almost always accompanied by a subnormal temperature, a rapid soft pulse of low tension, a desiccated skin, soft eyeballs and an abnormal type of respiration varying from the slightest hyperpnea to most outspoken air-hunger. No patient in diabetic coma has a urine which does not contain sugar; albumin and showers of casts are frequently found. Acetone and diacetic acid may both be absent although both acids are usually present in large amounts. A well-trained nose can often detect the fruity acetone breath. Many cases seem to develop acidosis acutely with such initial symptoms as nausea, vomiting, abdominal cramps, restlessness and finally air-hunger. An antecedent history of diabetes is not necessary. Finally, most people are not introspective and all cannot state the onset of their illness with any accuracy: Many mothers do not know whether their comatose child has lost weight recently,

has been excessively hungry or thirsty, or even whether he has had a normal bowel movement in the last two or three days. Therefore, one must always exclude diabetic coma by urinalysis in a patient presenting any of the clinical signs of acidosis.

If diabetic coma does develop, the patient must be safe-guarded from infection in every possible way and given insulin. The patient must be kept in bed and must be kept warm; he should be given an enema at once; and plenty of fluid by mouth or rectum. If the stomach is not upset, a diet of orange-juice and gruel is satisfactory until the insulin arrives. Comatose cases often require considerably more insulin than other cases, therefore the drug must be given in relatively large amounts. It is safer for the patient to have a messenger bring insulin from the hospital rather than for the patient to go to the hospital for treatment and develop a fatal septicemia on the way by getting chilled and shaken up in an ambulance, especially because the home treatment of coma with insulin is perfectly safe and requires no more laboratory equipment than some Benedict's solution, a medicine dropper and a test-tube. After the emergency is over, the case can be hospitalized, if necessary, for purposes of education.

Sepsis is in many cases preventable through education. Diabetics must be taught to take care of themselves in every reasonable way. They must be told the possible significance of acute respiratory diseases, of intestinal infections, of skin infections, of chronic dental and tonsillar infections; they must learn to protect themselves from overexposure to cold and dampness, from overwork and worry. Finally, they must learn that infections of any sort invariably lower tolerance and that repeated minor infections can make a mild diabetic rapidly develop into one of great severity.

Cardiovascular or renal disease including gangrene often cause death in diabetes. Unfortunately cardiovascular and renal disease are very common in people past the middle period of life. Fortunately diabetes in this type of individual is usually mild, the patients are often obese and a low-protein low-calory diabetic diet is as good for the one disease as for the other. A mistake which we personally have been guilty of in the treatment of this type of case, however, is to discover the existence of diabetes through a routine urine analysis, thus have our attention focussed upon the blood or urine sugar, and as a result disregard the coexistence of what was a much more serious heart or kidney disturbance. In protecting this particular sort of case, therefore, one must remember the importance of diet for glycosuria, rest and digitalis for heart disease, limitation of fluid and salt intake for kidney disease, and above all the necessity of a systematic plan of life with prescribed diet, rest, exercise, and medication, and a due consideration of all the factors in this combination of diseases.

Gangrene is so common and so unnecessary in diabetics that as

Joslin has inferred, we should coöperate to organize an antigangrene campaign. Dr. Joslin's rules for care of the feet as a means for the prevention and treatment of this complication are inserted as being of the greatest practical value. We believe they should be enforced in all hospitals where diabetics are treated.

Joslin's Rules for the Treatment of the Feet in Diabetes. *General Hygiene.* 1. Wash the feet daily with soap and water. Dry them thoroughly, especially between the toes.

2. When the feet are thoroughly dry, rub them well with hydrous lanolin, as often as is necessary to keep the skin soft, supple and free from scales and dryness. If the nails are brittle and dry, soften them by soaking them in warm water a half hour each night and apply lanolin generously under and about the nails. Then bandage the feet loosely. The nails should be cleaned with orange-wood sticks. Cut the nails straight across and avoid injury to the toes.

3. Wear shoes which do not bind or rub. Wear new shoes one-half hour only on the first day and increase one hour daily.

Treatment of Abrasions. 1. In the diabetic, insignificant injuries may result very seriously, therefore proper first-aid treatment of any abrasion is of the utmost importance.

2. Thorough cleanliness with soap and water is necessary.

3. Strong irritating antiseptics such as sulphonapthol and iodin are to be avoided.

4. The lesion should be covered with lanolin on sterile gauze under a slight bandage. Sterile gauze in small packages can be purchased at drug stores.

5. Avoid using the foot as much as possible until the wound is healed.

6. The patient must consult a doctor for any infection.

Treatment of Corns and Callosities. 1. Wear shoes which cause no pressure.

2. Soak the affected foot in warm, soapy water. Dry and rub or file off any dead skin. Then paint the corn with the following mixture: Salicylic acid, 1 dram, collodion, 1 ounce. Repeat the procedure for four nights, then, after soaking the foot in warm water, the corn will come off easily.

3. Do not cut corns or callosities.

4. Wear a pad to distribute pressure, if necessary.

Circulatory Aids. 1. Prescribed exercise.

2. Avoid *sudden* changes in temperature.

3. If the feet are subject to chilblains, wash them daily in *warm* water, dry them carefully and powder them lightly with borated talcum powder. Wear woolen stockings and avoid extremes of temperature.

4. Massage with lanolin.

5. Buerger's gravity—hyperemia method for bed-patients.

Conditions Requiring Attention in Diabetic Feet. 1. Cold feet.
2. Dry, scaling, atrophic skin.
3. Thick, dry, brittle nails.
4. Corns and callosities.
5. Cramps.
6. Stiff or limited joints.
7. Discoloration with red or bluish areas.
8. Clammy, moist skin.

Pulmonary tuberculosis judging by our necropsy material is fairly common. Out of about 1000 postmortem examinations in this hospital, active pulmonary tuberculosis was found in approximately 6 per cent; out of 42 diabetic necropsies active pulmonary tuberculosis was found in 16 per cent. Therefore active tuberculosis proved to be more than twice as common among the diabetics as among the patients as a whole. Since insulin appears to offer the tuberculous diabetic the same chance of recovery as would exist were the tuberculosis not complicated by diabetes, vigorous treatment for both conditions should be followed out in all cases.

The chief difficulty in this combination of diseases rests in diagnosis: Pulmonary tuberculosis is easily masked by diabetes and may be completely overlooked on ordinary physical examination. We believe that all diabetics, and specially those under forty years of age, should have routine roentgen-ray examination of the chest to exclude any pulmonary disorder. The necessity for this procedure will be made plain in a subsequent review of our tuberculous cases.

Conclusion. On the whole, insulin opens up so many new possibilities for the future treatment of diabetes that we believe it more important than ever to learn as much as possible from well-studied fatal cases. Therefore, we have presented this review of the cases of the medical clinic of the Peter Bent Brigham Hospital.

This study has justified the following conclusions: There were 4 common causes of death in the cases of this series and they represent the common causes of death in diabetes described by other authors. These causes are: Coma, sepsis, cardiovascular disease including gangrene, and pulmonary tuberculosis. Many diabetic deaths can be prevented and many diabetic lives can be happily prolonged if these causes are generally recognized and prevented or treated in their early development. A serious effort should be made through education to protect diabetic patients from the dangers—of coma, sepsis, and gangrene. Diabetic coma should be recognized at the time of its onset and treated before a terminal infection develops. Diabetics with cardiovascular and renal disorders should be as systematically treated for diseases of the heart, kidney or arteries as for diabetes. Pulmonary tuberculosis complicating diabetes should be discovered before it becomes hopelessly advanced, and both diseases when coexistent should be treated hopefully and vigorously.

THE OCCURRENCE OF HERPES ZOSTER IN HODGKIN'S DISEASE.*

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The occurrence of herpetiform eruptions in Hodgkin's disease is a rare condition, but it does occur more frequently than is generally recognized or taught. In reviewing the literature on Hodgkin's disease, the authors were unable to find a single instance in which mention was made of the occurrence of herpes zoster in the disease or as one of the skin complications.

After reviewing some of the literature concerning herpes zoster, we found one illustration[1] where herpes occurred in connection with Hodgkin's disease, but no other record of the case was reported. However, there were several reports of cases of malignancy which were complicated by herpes zoster during the course of the disease. It seems wise, therefore, to review some of the theories of the causes of herpes zoster in connection with this report.

In 1864, Mitchell, Morehouse and Keen[2] showed that irritation and not section of a nerve was the cause of zoster and similar eruptions. Later it was shown that compression by tumors, etc., might result in zoster along the distribution of the implicated nerve.

The simplest and most plausible theory of the production of zoster, and one, indeed, which must account for a certain number of cases, is that of propagated neuritis. This supposes that zoster is simply the result of an inflammatory irritation transmitted by continuity of tissue from a nerve twig, or branch, to the cutaneous elements among which it is distributed.

Cancer, otherwise than through the direct influence of pressure from the new growth, has been suggested as a cause of zoster. Cassière,[3] in a case of femoro-cutaneous zoster following cancer of the uterus, found parenchymatous neuritis of the nerve involved. There was no cancerous infiltration of the nerve, and Cassière attributed the neuritis to the local and direct action of cancer toxins. One of Dr. Curtin's cases was also connected with cancer of the esophagus.

Head and Campbell,[4] in a recent and extremely elaborate paper, give a large number of facts regarding the origin and distribution of zoster. These investigators have been able to map out the affected areas in zoster and have subsequently examined the spinal cord

* Presented before the Pathological Society of Philadelphia, May 10, 1923.

and nerves implicated. They find inflammatory and destructive changes in the posterior ganglia of the cord and in the Gasserian ganglion, and degeneration in the nerves leading to the skin. In mild cases the effects of these changes gradually pass away, but in severe cases the nerve fibers that have degenerated are replaced by fibrous tissue, and whole bundles of the nerves may be sclerosed. Head and Campbell conclude that some agent, the nature of which we are ignorant, chooses the substance of the posterior root ganglion for its selected activity, producing profound inflammatory changes. These destructive changes in the ganglion give rise to irritation of its nerve elements, and to this irritation is due the eruption on the skin.

Case 14 in the series reported by Head and Campbell[4] was a male, aged forty years, who seventeen days before death had a severe herpetic eruption over the 4th dorsal area. At the postmortem examination a mass of glands in the posterior mediastinum was profoundly affected by new growth passing in along the nerve sheaths through the foramina. The 4th dorsal ganglion was in the midst of lymphosarcoma tissue.

They also state, "It is well known that when the secondary deposits of malignant disease attack the spinal column the pain produced becomes intense. It is, however, less a matter of common knowledge than an eruption indistinguishable from that of zoster may also make its appearance. Charcot and Cutard gave a very insufficient report of such a case in 1865, but we can find but one other paper dealing with this subject, Riesel."

Hall[16] in discussing the complications of new growths within the chest states that herpes zoster occasionally occurs along the nerve compressed by a new growth.

Thus one can readily observe that zoster does occur in patients having new growths, and although there are only a few reports on record, there are probably a number of other cases that have not been reported. Then too, most of the malignant cases are ambulatory, and one often does not see them except at long intervals, thus missing an acute attack of a condition such as zoster. There are recorded below 4 such cases occurring in Hodgkin's disease and 1 case of herpes zoster occurring in sarcoma of both ovaries. We feel that we have seen several times this number but due to incompleteness of our records, we are only able to report 5 definite cases.

Case Reports.—CASE I.—M. C., a female, aged twenty-seven years, married, was admitted to the University Hospital January 25, 1921, with the diagnosis of Hodgkin's disease.

H. P. I. In March, 1920, the patient had a sore throat and was in bed for a week. Two days later a lump developed on the left side of the neck, which slowly grew larger to the size of a hen's egg. Within a few months, involvement of the left epitrochlear, left

axillary, left preauricular and inguinal nodes became noticeable. The size of the glands varied from time to time. Since the beginning of the disease the patient has had a severe pruritus. At times she had fever and perspired freely. The glands gradually increased in size since first noticed.

Physical Examination. The skin was dark and showed numerous scratch marks. There was a general adenopathy especially in the axillæ, neck and groins, the glandular masses under the arms being about the size of an orange. The spleen was palpated and extended about 6 cm. below the costal margin. The inguinal adenopathy was more marked on the right side, the glands being about the size of walnuts. The blood counts were as follows: Red blood cells, 3,190,000; white blood cells, 32,000; hemoglobin, 55 per cent; differential polymorphonuclears, 87.5 per cent; lymphocytes, 8.5 per cent; large mononuclears 2 per cent; transitionals 1.5 per cent; myelocytes 0.5 per cent. The patient's temperature was elevated daily. The blood Wassermann test was negative. A pathological examination made by Dr. Fox revealed Hodgkin's disease. Roentgen-ray treatment was commenced and the patient received a general radiation over the body from February 11, 1920 to June 10, 1921. On July 25, 1921, the patient came in complaining of considerable pain in the right kidney region which was treated by roentgen-ray and radium with a temporary improvement. However, on October 26, 1921, the patient returned complaining of the same pain and shortly after developed a typical lumbar zoster of the hemorrhagic variety. The patient was again treated but without any beneficial results and later died.

Summary. A typical case of Hodgkin's disease with skin manifestations of herpes zoster late in the course of the disease at which time there were definitely enlarged glands palpable in the kidney region on the right side.

Case II.—P. B., a female, aged ten years, was admitted to the University Hospital November 30, 1917. The patient at that time had an enlarged mass of glands on the left side of the neck. These were removed by operation, and the enlargement was shown by microscopical examination to be caused by Hodgkin's disease. There was a palpable gland in the right axilla and the spleen was enlarged about 6 cm. below the costal margin. A roentgen-ray examination of the chest was negative for any definite involvement of the mediastinal glands. The patient was treated at varying intervals by crossfire radiation of roentgen-rays. On February 6, 1923, the patient returned to the hospital in a very weak and anemic condition. The glands in the axillæ, neck, inguinal and pelvic regions were considerably enlarged. A roentgen-ray examination of the chest did not reveal any definite enlargement of the mediastinal glands. The patient had a band of scars extending around the chest which were

typical scars of herpes except where some had undergone keloid formation. The patient stated she had had "shingles" two months

FIG. 1.—Case II. Anterior view, showing the eruption extending as far as the midline of the body.

FIG. 2.—Case III. Lateral view, showing the eruption in the axillary regions with quite definite keloid formations.

before admission to the hospital on February 6, 1923. The patient was given another series of treatment, is living and in fair condition today. (See Figs. 1 and 2.)

Summary. Hodgkin's disease; occurrence of intercostal herpes zoster (right side of thorax); late in the infection and without any demonstrable mediastinal enlargement.

FIG. 3.—Case II. Posterior view, showing the scars extending as far as the midline of the body with even more definite keloid formation.

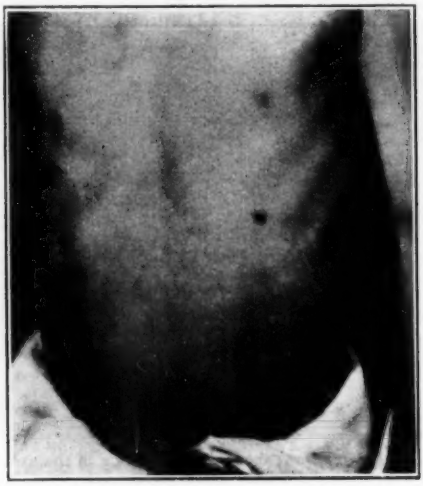

FIG. 4.—Case III. Anterior view, showing the small scars extending as far as the midline.

CASE III.—A. P., male, aged nine years, was admitted to the University Hospital January 7, 1921. Two years ago the glands in the right

side of the neck began to enlarge. For sometime the glands remained the same size but later they began to fluctuate in size and the patient developed fever. At the present time the patient has a glandular enlargement on the right side of the neck, anteriorly, and to a less extent on the left side. The posterior cervical chain is distinctly palpable. Numerous glands are palpated in both axillæ. The spleen is palpable slightly below the costal margin. The inguinal nodes are enlarged. The blood count was as follows: Red blood cells, 3,200,000; white blood cells, 4,700; Hemglobin, 40 per cent. The von Pirquet test for human and bovine tubercle bacilli was negative. A roentgen-ray examination of the chest showed a mediastinal tumor. A microscopical examination of the gland removed from the neck showed characteristics of Hodgkin's disease (Dorothy Reed type). The patient received treatment by crossfiring applications of roentgen-rays over the involved areas.

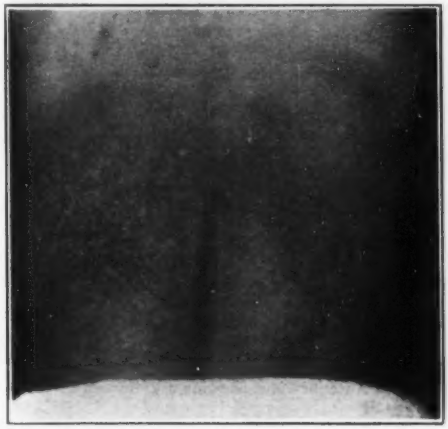

FIG. 5.—Case III. Posterior view of same patient as in Fig. 4.

On April 23, 1921, the patient developed a herpes zoster eruption involving the 9th, 10th and 11th intercostal nerves on the left side. A roentgen-ray examination of the chest at that time showed prominent hilum shadows. The patient is still under observation and doing well. (See Figs. 3 and 4.)

CASE IV.—R. S., female, aged forty-nine years, was admitted to the University Hospital, July 16, 1917. The patient first noticed enlargements on each side of the neck, the axilla and the groin in October, 1916. A roentgen-ray examination of the chest at that time showed mediastinal enlargement. Later the patient developed nodular enlargements over the scalp and an exophthalmos of the left

eye which was thought to be due to an intraorbital growth. After roentgen-ray treatment over these areas, the nodules and the exophthalmos disappeared. These areas have been treated from time to time and the patient continues to remain in good health. In December, 1920, the patient developed a right femoro-cutaneal herpes. Examination at that time failed to reveal any glandular enlargement in the inguinal or the pelvic regions.

Summary. Hodgkin's disease with occurrence of herpes zoster along distribution of right femoro-cutaneal nerve. It occurred late in the affection and at the time no demonstrable enlargements could be palpated.

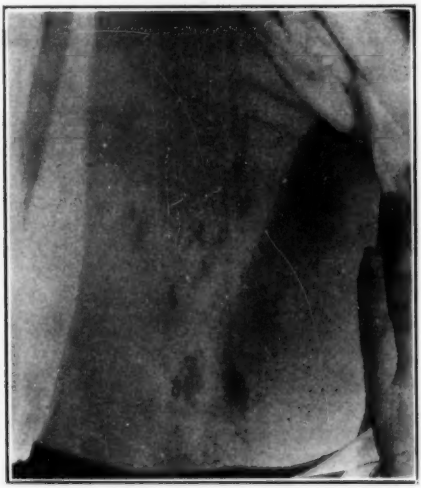

FIG. 6.—Case V. Anterior view, showing eruption under breast, left side.

CASE V.—C. S., female, aged twenty-seven years, was admitted to the University Hospital August 16, 1921. The patient noticed a lump on the left side three months before admission. Very soon after its appearance the lump began to cause considerable pain. The patient was operated on and a bilateral salpingo-oöphorectomy and supravaginal hysterectomy performed. It was found at operation that there was a general peritoneal metastasis. The pathological report was sarcoma. Later, the patient developed a mediastinal metastasis and also metastasis to the region of Ewald's gland. Under roentgen-ray treatment the patient improved and is living and well at the present writing.

On May 15, 1923, the patient developed a severe herpes zoster which involved the distribution of the 11th and 12th intercostal and 1st lumbar nerves on the left side. (See Figs. 5 and 6.)

Summary. Ovarian sarcoma with extensive metastasis. Patient developed herpes zoster involving the 11th and 12th intercostal and the 1st lumbar nerves, left side. A roentgen-ray examination of the chest and spine was negative for any evidence of growth.

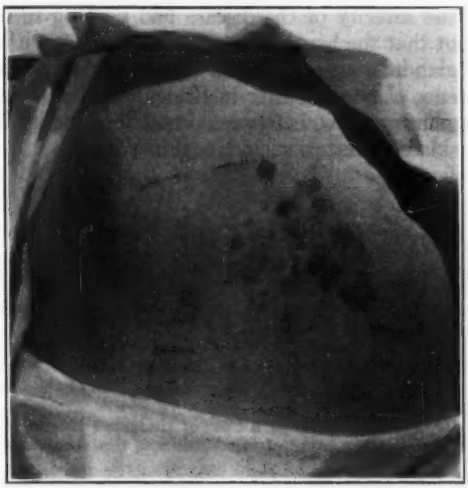

FIG. 7.—Case V. Posterior view, showing eruption on back.

Comments. In Case I, the zoster was typical and occurred on the right side. A large mass could be palpated in the kidney region, posteriorly, on the right side. The active eruption lasted about eight weeks.

In Case II, the zoster occurred on the right side of the chest. Another interesting feature of this case was the keloid formation resulting from the zoster lesions. At the time of the eruption there was no definite mediastinal mass demonstrable by the roentgen-ray. This case of zoster was rather severe.

In Case III, the patient had a light attack of zoster on the left side of the chest. At the time of the attack the hilum shadows were enlarged.

In Case IV, the patient had a slight form of herpetic eruptions which disappeared in five weeks. No enlargement could be palpated at the time of the eruption.

In Case V, the patient had a severe and painful eruption which lasted for eight weeks. The patient has been unusual in that she has responded so well to roentgen-ray treatment in spite of the extensive involvement.

Summary. There are reported 4 cases of Hodgkin's disease and 1 case of ovarian sarcoma in which there occurred an attack of herpes zoster during the course of the disease.

In none of these cases were autopsies performed. The first case died of Hodgkin's disease, the zoster occurring rather late in the affection. In the last 4 cases, which are still under observation, the zoster occurred rather early during the course of the disease in 3 and late in the other. Judging from these cases alone, it would seem that the severity of the disease had nothing to do with the eruption, but that the herpes was probably due to irritation caused by mass of glandular enlargement in close proximity to the ganglion. The occurrence of herpes zoster in Hodgkin's disease, as well as in other malignant growths, is frequent enough to justify its inclusion among the skin manifestations in Hodgkin's disease.

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THE EFFECT OF MALARIA ON THE NERVOUS SYSTEM WITH SPECIAL REFERENCE TO THE MALARIAL PSYCHOSES.

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Historically, Sydenham and Hoffman were the first to point out the psychic troubles of "intermittent fever." Cases of malaria

with mental symptoms observed since the earliest history of the disease are to be found in the literature reported as "an unusual manifestation, a rare case of malaria," and so forth, and unfortunately many of the observations given, though none the less honest, were by men not trained in psychiatry. While the malignant tertian organism (Plasmodium falciparum of Blanchard) is generally conceded to be the etiological factor in cerebral manifestations of the disease, from this treatise one finds that, other than infection, there are many factors associated with this, the most dreaded malarial hematozoön, which are productive of mental symptoms.

The type of mental reaction depends upon the acuteness or chronicity of the disease. Somewhat similar to the delirious case of frank lobar pneumonia incarcerated for alcoholic intoxication, the delirium[1] of undiagnosed malaria may be taken for the acute onset of a psychosis and commitment to an asylum, if not carried out, may at least be contemplated. The onset has been found to be very abrupt, occurring even while a person was walking along the street. This may be understood[2] since infection causes mental disturbances before the rise in temperature occurs, and often delirium subsides after fever has set in. Although this is not the rule, this type of reaction has been observed in malaria. Skliar[3] has recently remarked that there are two infectious diseases in which delirium is observed without rise of temperature, namely, malaria and certain stages of variola. Hyperpyrexia following the infection may either cause delirium *per se*, or enhance the picture already present.

Papastratigakis[4] states that in acute malaria, periods of anguish are intimately connected with the attacks of fever. The patients, without being confused, are a prey to the most distressing anguish, which is not always proportionate to the degree of fever elevation. They have the impression of approaching death and their faces express the condition of a person in great fear. This condition is quite transient, disappearing with the first drops of sweat, and giving place to a characteristic euphoria.

Since it has been observed that the several types of malaria are not infrequently complicated by mental symptoms, no attempt will be made to lay stress upon any particular organism. Sufficient that we recognize plasmodia and the toxins secreted by them, pigment, chemical action of the disintegration of red cells and intoxication due to insufficiency of liver and kidneys in any case of malaria.

To understand the psychoses associated with malaria, I have chosen to attack the problem by treating all the mental observations in the order frequently exhibited by the patient, that is, initial delirium, with or without coma, the psychoses "typical" of malaria with subsequent amnesia; chronic malarial psychosis; pathology of the nervous system in malaria; cerebral malaria with aphasia as

one of its important complications; neurological manifestations and such states as neurasthenia, epilepsy and hysteria.

Initial Delirium. Régis[5] says that the psychic troubles of the febrile attack consist in an hallucinatory mental confusion of variable acuteness. In the lightest degree there is a sort of subdelirium without total loss of consciousness rather than a true delirium, coming on principally with the period of fever and disappearing shortly afterward in the period of sweating.

At a higher degree the dream-like delirium is realized in the clearest and most typical form. But it is still possible by a brisk agitation, an energetic interpolation, to bring the patients out of their delirium for an instant and to lead them to reality. Ponty[5] gives his personal experience during the numerous attacks of fever he suffered in Madagascar, and says: "This very clear sensation of awakening at a brisk appeal I have myself felt very plainly and a typical thing, one recalls his delirium, one recounts it like a dream." At this degree the delirium is longer. It persists to the end of the fever and may even prolong itself beyond the period of pyrexia. It is not rare to see it reappear, exactly in the same condition and under the same form, at each new attack.

The delirium may be still more intense, with crying, disordered acts, violence and agitation. It often terminates with death, in convulsions and coma.

Delirium in a pernicious chill attack, although more rare than in the initial periods, was observed by Ponty. The case cited was in a sergeant major who had a typical professional delirium, during which time he lived again his routine army life, such as giving commands, drilling and so forth, ending in death within five hours.

Probably the best contribution to the study of malarial delirium is that of Jean Lecler.[6] His observations were made at Saloniki in a general medical service where these deliria run their course without the necessity of evacuating the patients to a psychiatric center.

Except for one observation, the clinical picture is constant, at once dreamy and confusional; one finds again disorientation, the hallucinations of action, often professional, the return to reality after an energetic interpolation; then the headaches, the psychic fatigue and the amnesia for the delirium.

Lecler thinks that the mental distress, spontaneous or on palpation of the liver and spleen, is important; for he believes the sense of weight and distress, due to the swelling of these organs, may give rise to misinterpretations on the part of the patient, and hence he explains in part disturbances of sensibility which carry the person affected with malaria toward serious delirium. The state of the liver and its functions merit a longer study, which would explain the similarity of the malarial and alcoholic deliria, as well as the easy alcoholization of malarial cases. Therein lies an etiological

factor in mental disturbances associated with malaria, whether they are short-lived delirious states or whether they progress to a psychotic episode.

Folly's[7] observation upon the role of alcoholism in malarial delirium is valuable. In general, he found that delirium occurred in pernicious forms of the disease; that the initial malarial delirium did not exist in Arabs; that it was only found among alcoholic Europeans. Since the Arabs abstain from alcoholic drinks, save a few natives of cities, and as a class the Arabs are free from the initial malarial delirium, while, on the other hand, the European users of alcohol as a general rule suffer the initial delirium, the reasonable assumption is that alcoholic intoxication is closely associated with and is responsible for the initial malarial delirium to a large extent. Similarly, he found in the Zouaves stationed in malarial districts who were still too young to be deeply alcoholic that, with some exceptions, they too escaped the initial malarial delirium. With Europeans of Algeria, Folly says, the delirium, one might say, is the sign of alcoholism, and in fact inquiry that we have made has always confirmed our preformed opinion. Bearing in mind the frequency of nephritis in malaria, and the possibility of its being complicated by uremia, Folly was careful to eliminate such cases of delirium, and almost all of his cases were of true malarial origin.

As to the types of delirium met with, there were three: It was sometimes pure delirium tremens, sometimes an incoherent delirium with professional hallucinations, sometimes an agitated delirium with epileptiform convulsions.

Régis states that dream-like delirium is not a psychopathic reaction peculiar to alcohol, but represents the characteristic expression of all the intoxications and infections of the organism. Not only from the direct impregnation of the patient's entire body with the malarial toxic injection, but peculiarly due to the insufficiency of the various secretions, particularly of the liver and kidney, do the varied clinical manifestations of intoxication present a similar symptomatological picture.

Coma Following Delirium. The delirious malarial patient may or may not merge into a comatose state, which in turn may end in death or recovery. In considering coma it is to be remembered that while any variety of malarial plasmodium may give rise to this manifestation, the vast majority of cases are due to the estivo-autumnal parasite. Aside from preëxisting conditions in the individual, such as anemia, cachexia, physical or mental fatigue, the puerperium, insolation and alcoholism, the development of coma depends upon three factors: The number of parasites present, the amount of toxin secreted by them and, most of all, the localization in the brain.

Many cases of comatose malaria are reported. Neer[8] reports 3 cases, 2 having come to autopsy showing the usual findings in the

brain, and a third case of typical estivoautumnal infection without postmortem examination. He states that coma may come on suddenly, like an apoplectic stroke, or may begin gradually during a paroxysm of fever, preceded by slight disturbances in the sensorium, such as apathy, somnolence, restlessness and melancholia. The coma may disappear with the fall of temperature, to reappear again within twelve to twenty-four hours, or it may continue over a period of one to four days, until death or recovery ensues. Tresidder[9] reports a case of malarial coma lasting forty-six hours, with recovery. The attack was accompanied by epileptiform convulsions and followed by restlessness, delusions of persecution and incoherent speech. The patient recovered mentally within six days. Quaife[10] reports a case of cerebral malaria with recovery after forty-eight hours of unconsciousness. It occurred in a boy, aged eighteen years, employed on a small sailing vessel. He suddenly fell down with violent convulsions and deep unconsciousness. Fresh films of blood showed a few half-grown pigmented malarial tertian parasites. Complete recovery without any complications followed quininization. Graham's[11] case was as follows: The patient felt "seedy;" toxic spasms started which became so violent that it was necessary to administer chloroform; there was a period of hyperpyrexia, with blood negative for parasites, and an unconscious period lasting two days. The patient had delusions of persecution for the following two weeks, but eventually recovered. Knowles[12] reports a case of coma in a young Hindu woman which lasted two days, after which, with a period of pyrexia, aphasia developed. Thomson[13] reports a case which developed suddenly in a laborer while digging in a ditch, whose blood was found to contain many benign tertian parasites.

"Typical" Psychosis. Psychoses, *per se*, have been observed repeatedly, both accompanying the attack and as sequelæ. Ascoli[14] says that psychoses from malaria are extremely rare. In the Manicomio, at Rome, they range at the highest 0.5 to 1 per cent. Ascoli, who has probably done more work in malaria than anyone else, sums up his opinion in saying: "Clinical experience demonstrates, then, that malaria causes disturbed (transitory) states of mind, at times also grave ones in its acute onset, that it is able to leave the organism more or less depressed and asthenic, but that of itself it does not give place either to a neurosis or psychosis proper." The frequency of neuroses or psychoses, as Chavigny asserts, is slight, and Kraepelin affirms that they are more frequent in women than in men. The mass of data upon malarial psychoses is large and diverse, due to the facts that the disease infects so great a number of people in both sexes and of all ages, each with his individual personality make-up, and that there are many external factors. To enumerate some of these: Von Krafft-Ebbing[15] saw a case manifesting typical paroxysms of intermittent fever

until after a blow on the head, when an intermittent psychosis with the syndrome of epileptic confusion set in. Manson[16] cites the case of a man who came from Bombay to London, and was placed in an insane asylum on account of symptoms of insanity. Blood examination revealed the diagnosis.

Segard[17] reports several cases of psychic disturbances. In one acute mania with erotic outbreaks lasted three days after a malarial coma of fifty-two hours' duration. In another case a soldier, while recovering from fever, became obsessed with the idea that he was needed at the post, and in an attempt to get there met death by drowning. In a third case a man, who had stood several ordinary paroxysms, one evening during a paroxysm was seized with hallucinations, rushed out and wandered around in the thicket all night.

Pasmanik[18] seems to have had wide experience with malarial psychoses. Among 5412 malarial cases he found mental disturbance 106 times. An hereditary influence was present in none of these cases, and alcoholism in 4.8 per cent. All the cases were depressed. Their duration varied between four days and three months, except in one case of persistent dementia. Pasmanik found soporose conditions to be the most common in children. On exacerbation of chronic malaria melancholia arose and the worst prognosis was in the delirium of cachectics, the result of a relapse.

Gehrenstein[19] found depression most often in malarial psychoses.

"Case I.—Patient, female, aged thirty-three years; complaining of severe headache, continuously; depression, even to suicide at times; other days she feels better, and performs her usual tasks. When depression gets the best of her she throws everything aside, secludes herself from relatives, sits and prays for hours for her sins. Believes God is punishing her. She begs forgiveness from her neighbors and relatives for insults to them, and repents of her sins. She suffers from insomnia. According to her husband, such periods of severe depression are followed and changed by periods of bettered condition, when she becomes more energetic, works and gives no evidence of depression.

"History showed that in former years she suffered a fever, typical chill, followed by feeling of heat and perspiration.

"Spleen enlarged; palpable to the left under the ribs. Temperature normal; pulse, 72. Laboratory examination for plasmodium on one occasion was negative. However, taking into account the facts of the history, physical and mental, 0.6 gr. quinin hydrochloride, three times a day, was prescribed.

"After having taken 4 gr. the patient returned, stating that in all these days she felt real well; attacks of depression passed, appetite increased and sleep was present. In other words, a noticeable change for the better took place. Following this I did not see her any more, but, according to information, she has improved altogether.

"CASE II.—Patient, aged seventeen years. Mother states the patient has been ill for over a week, constantly going away from relatives and friends, keeping silent to such an extent that even the most insistent questions elicited a reply with very great difficulty. Very passive toward everything, even to her most natural wants. She was liable to sit a whole day without food or drink unless offered her. Answered questions with very marked unwillingness and expressed dissatisfaction, making, when anyone wished to enter conversation, an effort to go away. If persistently questioned she complained of depression and pain. Sometimes she would pace the floor and murmur something for hours in succession. Expression melancholic. Internal organs show no deviation from normal. Menstrual periods normal. No psychopathic heredity noted. According to the mother, the girl suffered all the spring of this year with fever of tertian type. Laboratory examination on the first occasion revealed plasmodia of malaria. Given 0.5 gr. of quinin hydrochloride, three times a day, for four days, with the request for a report at the end of this time. She came to the dispensary much to my surprise alone—happy, full of life, not at all like the girl I had seen a short while ago. Subsequently the condition has not returned.

"CASE III.—Patient, male, aged fifty-two years. Treated him previously for chronic bronchitis; one week ago he suffered for three days with an intermittent fever. The daily attacks have disappeared after medication with quinin. Soon after the disappearance of attacks the patient fell into a dark depression, crying at times, certain that he was suffering with consumption and must die soon. No efforts on my part and those of relatives to convince him that his opinion was all wrong and baseless were effective, and he was insisting upon his early end. He would closely inspect his sputum and would find suspicious symptoms which only he could note. Suffered insomnia, refused food, passed all the time in introspection following his every sensation. Prescribed bromide and chloral and warm baths, but these had little effect on his disposition.

"Temperature during my visits was normal; spleen enlarged but not palpable from under the ribs. With the exception of the already mentioned chronic bronchitis, internal organs revealed no pathological changes. Laboratory examination for plasmodia on two separate occasions gave positive results. Assured then that this was a picture of marked malaria in the form of a psychosis, I prescribed 2 gr. quinin per day for three days, and it could be observed how soon the above described condition was passing. The patient was becoming more energetic and happy. The thoughts that formerly depressed him now looked to him ridiculous. Sleep and appetite better. In a word, this patient after having quinin

went on the road to recovery, although some time after he passed again through two or three typical attacks of intermittent fever.

"CASE IV.—Patient, female, aged twenty-six years, came to the dispensary complaining of precardial depression, which had continued for two weeks. She says that this feeling is so painful and unbearable that she feels herself out of place everywhere; cannot get down to any work, has neglected housework, ceased taking care of her nursing baby and is obsessed by the idea that all this is probably a punishment sent from Heaven for her sins, crying and becoming more and more introspective; according to her husband, the patient showed a very marked change and has turned from heretofore an energetic and good worker to an indolent woman who for hours in succession spoke only of her sin and cried all the time. The expression of the patient is that of misery, frequently sighing and crying. Appetite and sleep absent.

"Temperature normal; spleen slightly increased. Information given by her husband is to the effect that previously the patient suffered attacks of intermittent fever that would pass after taking quinin. Laboratory examination of the blood was negative. Three days' medication with 2 gr. quinin hydrochloride per day brought about a marvelous effect. All the depressive symptoms that tortured the patient have passed. Appetite and sleep appeared; an interest was created in her daily tasks and she returned to work.

"Conclusions: Analyzing these instances, let us note that the psychosis is of a depressive nature. In the first and fourth cases the psychosis appeared in the form of depression with delirium; in the second case melancholic, with stupefaction (Melancholia atonita); and finally in the third case it reminded one of hypochondriacal melancholia.

"The preponderance of melancholia in malarial psychoses is difficult to explain except perhaps as observed by me, as well as others, that most of my observations were among women and not in men, and it has been established by others that melancholia is three times as frequent in women as in men.

"Malarial psychoses, by reason of their rarity, might easily escape the attention of a physician and be taken for psychoses, having altogether different etiology."

Chavigny[20] states that infection gives rise to varied nervous and mental complications, and the only thing that proves them to be of malarial origin is that quinin cures. There is a disputed question of the relative etiological importance of three factors very difficult to dissociate, namely, predisposition, alcoholism and malaria. He believes these three to be the constant antecedents and further states that it may in part be observed that there is an

exact superposition of the development curve of these psychoses on that of alcoholic intoxication. Finally, he gives as the theory of causation of malarial psychoses that malarial delirium is a toxic delirium, that alcoholism favors the production of the seizures, and that the heredity has prepared a favorable soil for the intoxication.

Régis has observed psychic attacks in subjects of perfect sobriety and Rey affirms the possible absence of every predisposition.

Malarial psychoses, properly so-called, usually take the form, as Régis has shown, of mental confusion or a dream delirium. Clinically, they cannot be distinguished from psychic seizures of alcoholic origin, that is, nocturnal hallucinatory delirium with visions of occupations of terrifying nature. However, hysteria may be set in activity by malaria. Epilepsy, often observed, should be distinguished from uremic convulsions. Neurasthenia is frequent and may take the form of masked seizures or of sequelæ. These three states will be discussed later.

Parot and Gutmann[21] have done rather extensive work with psychoses caused by malarial infection and consider the mental confusional state to be the initial psychopathy in malaria. Their observations[22] were made on Orientals and malarial patients from the north of Africa, and they ignored the acute but ephemeral mental symptoms, which sometimes accompany malarial attacks or act as their equivalents, such as transient oniric attacks, flights, crises of amnesic delirium, hysteriform mimic reactions. These they considered not real psychopathies, but epiphenomena. Although most of the mental syndromes found in malaria are those of current psychiatry, these psychoses nevertheless have their own form, a little different physiognomy, explicable by the nature of the malarial infection and the physiological disorders which it brings on. They found that malarial psychoses are always, at the beginning, confusional psychoses; the confusion may change until it appears as a new syndrome; the stupor is transformed into a catatonic dementio; the oniric monoideism (dream-like delirium with one idea apparently uppermost in the patient's mind) becomes a chronic delirious psychosis. At other times the confusional storm appears in an exhausted organism, the psychic equilibrium of which is fragile, in great waves, maniacal or more often melancholic, which change it into a periodic psychosis.

Malarial mental confusion, which is often cured, is sometimes prolonged in a demential form (the chronic mental confusion of Régis); at other times it is transformed; but these secondary psychoses are always organized about sequelæ of the primary confusion, which represents the framework, final, transitory or temporary. The elements composing this syndrome at the beginning have been very carefully analyzed by Régis and Hesnard. The clinical picture includes the following: The confusional element, with its intellectual sluggishness, its bradypsychia predominating over the

oniric element, the dream delirium; with more sleep than dreaming; perception, orientation, consciousness very much disturbed; psychomotor agitation very slight; the delirium intermittent, not very sustained nor expansive, poor and monotonous. This predominance of asthenic and depressive symptoms, already striking, increases as the affection is prolonged. When the disorientation is dissipated and the awakening begins to take place the nervous exhaustion becomes still more apparent; it is at once both physical and psychical. A profound intellectual weakness, the absence of initiative, severe disturbances of memory, persistent, postoniric fixed ideas tinged especially with melancholy and a marked emotivity are frequent sequelæ which lead to error on account of the neuromuscular symptoms which often coexist. Disturbed reactions, maniacal conditions are sometimes observed, but much more rarely, and are the incontestable result of a constitutional predisposition.

They note the frequent coexistence of somatic nervous troubles, and state that the change in a patient's general condition is constant and serious, since the psychoses only make their appearance in deeply infected individuals.

In one of their typical cases reported a young man developed the syndrome of dementia precox within a year of contracting malaria in Macedonia. No other pathological antecedents were known in the personal or family history, except that he had convulsions as a child. In another case a man, aged thirty-seven years, developed acute mania, but under seven months of sanitarium treatment regained his mental poise, although still somewhat excitable.

Very valuable observations were made by Forrester[23] among the British Saloniki force. Malaria was the biggest factor in mental disease among these troops. It appeared that no new train of symptoms was set up by malaria, and that, in comparison with any other acute specific fever, it differed only in intensity and in the more selective action of its toxins on nerve tissue. The brunt of the attack falls upon the higher cortical centers, giving most commonly symptoms of acute confusion of a cerebral type. He describes two main classes, namely: (1) Psychoses associated with the actual malarial attack; (2) those occurring as a result of repeated attacks.

A study of 32 cases of the first class led him to believe that almost any of the recognized types of psychoses could be set up by the malarial parasite, but one symptom stands out prominently among them, namely, mental confusion. Next in frequency was depression. In every case a period of complete amnesia varying from a few hours to three months was noted. Only 4 of the above cases had hereditary factors.

In Forrester's 87 cases showing mental symptoms as the result

of repeated attacks 1 was returned to duty "not insane;" alcohol accounted for the mental disturbance in 7, while 9 suffered from varying degrees of feeblemindedness. In the remaining 70 cases in which malaria was the determining factor, it was found that any type of psychosis might be set up. The prominent symptom still was mental confusion; almost equally important in this series was that depression which one would expect to come as a result of prolonged stress and toxemia. Heredity played its role. Of the 24 cases of depression insanity in the family could be traced in 9 instances, while in 31 cases of confusion 7 showed a family history of insanity.

In regard to malarial mental confusion, Papastratigakis[4] has made his observations among young Greek soldiers who were without hereditary blemish and unacquainted with alcohol. He lays stress upon the abuse of quinin, in that it undoubtedly has a harmful influence on the psyche, and wonders that there is not any treatise in psychiatry on quininic psychoses. In fact, he believes the toxic action of quinin on the nervous elements exceeds by far that of alcohol.

As to confusional troubles, for which the author has proposed the name "malarial mental confusion," they may supervene in subjects without any predisposition, in whom malaria makes up the entire pathological past. Papastratigakis believes it to be essentially a toxic psychosis depending upon anemia and hepatorenal insufficiency. The essential character of the malarial mental confusion is that it is accompanied by certain symptoms which are habitually met in the course of confusions which evolve toward dementia precox, catatonia. Malarial confusion is a catatonic confusion susceptible of cure, which cure may arise between the sixth and eighteenth months. Two cases are cited.

This catatonic reaction was found in Jews as a race more frequently, and bears a definite relation to renal intoxication.

Besides catatonic phenomena, malarial confusion produces in the patient rather frequently aggressive tendencies toward his surroundings. It also causes at times a tendency toward ambulatory automatism. In the course of this confusion there may be noted hallucinations of taste and smell, quite similar to those of systematized psychoses and hypochondriac psychoses. They always accompany a bad functional condition of the digestive tract.

Subsequent Amnesia. Next we have to consider amnesia, which in malarial psychoses is commonly found, as in other infectious psychoses, following the period of initial confusion and more or less conditioned by it. Chabelle in a thesis gives numerous facts proving the frequency of dysamnesia in those affected by malaria, and in this way Régis says the malarial toxi-infection resembles very much infection psychoses where amnesia is, as one well knows, particularly marked.

Manson[24] has noted a loss of memory in cases of malarial polyneuritis, and M. H. de Brun[25] has of late found amnesia one of the most characteristic features of malarial polyneuritic psychoses. Of the cases studied at the Rueil Hospital almost a third of the patients had more or less impairment of memory. With a primary attack the memory of that period may be permanently a complete blank. One of his patients had no remembrance of anything connected with his stay in the hospital and for several months thereafter.

De Brun found that the malarial subject may also present retrograde amnesia, unable to remember certain periods in his previous life, possibly back into childhood. Some of the men had forgotten completely a foreign language which they had spoken fluently before contracting malaria. Others had forgotten historical events and geography or lost their knowledge of music or mathematics. Skilful electricians could not recall the most elementary principles of physics and electricity, and were unable to install the simplest electrical device. Artisans had forgotten the uses and names of tools.

Carlill[26] cites a case of Korsakow's psychosis conditioned by a malarial infection. Goodhart[27] cites a case of amnesia in a young school teacher who suffered an attack of malaria during which the accompanying mental symptoms, though mild, were typical. An amnesia for two days remained long after the malaria disappeared.

Chronic Malaria. In chronic malaria the associated psychoses have lost their more or less specific nature and the individual attacks are of shorter duration, though the tendency to recurrence is greater than after a single acute attack. They make their appearance as part of a relapse or may even replace the attacks as psychic equivalents.

Régis[5] states that invariably in chronic malaria the psychosis is preceded by localized headache. The malarial attack comes on with its clear stages of chill, pyrexia and perspiration or simply one of these, the chill stage in particular.

Delirium in these cases is a typical oniric delirium constituted by action, professional or fantastic, painful, terrifying, or approaching somnambulism. Régis has found in many of his cases that the delirium carries the patient back each time to the epoch of his life where he was taken with malaria, and often it is the same scene that comes back. Interesting are his cases of malaria in soldiers fighting their battles again, killing the enemy once more. As one would expect, disappearance of the delirium leaves the patient a little confused, stupid, with a certain degree of headache and an amnesia for the delirium more or less complete, according to the case.

Next in importance in the psychoses of chronic malaria are those which have for their basis physical and psychic asthenia. They

are those which follow one of the malarial neuroses, in particular neurasthenia, which will be considered later. The psychotic outbreaks, if there may be any sudden flaring up on symptoms, do not appear associated with a relapse of malaria, but rather in the form of a lasting psychosis with variable delirium (polymorphous). Régis has noted in chronic malaria what he chooses to term stupid mental confusion and dementia.

Pathology of the Nervous System in Malaria. To understand better the malarial psychoses let us consider briefly the pathological anatomy of the central nervous system in malaria.

Much has been written upon the pathogenesis of pernicious malaria; postmortem examinations in cases of cerebral malaria are rather uncommon; at least in the literature and from the facts deduced by numerous pathologists, divergent views are held as to the exact pathology. Deaderick mentions four factors which bear directly upon perniciousness: (1) An excessive number of parasites; (2) localization of parasites; (3) toxins secreted; (4) individual predisposition and external etiological influences.

As to the number of parasites, Golgi's law, that the number of parasites determines the severity of the attack, has been generally accepted. Marchiafava and Bignami[28] call attention to certain grave cases of comatose, convulsive, delirious or mixed pernicious malaria in which few parasites are found. This would indicate that there are other factors at work in the development of pernicious symptoms.

Localization of parasites may take place anywhere in the central nervous system. The plugging of perforating end arteries as found in the base of the brain and in the spinal cord would, of necessity, lead to the most serious symptoms. A more probable theory is that of Mannaberg,[29] who attributes the condition to a sort of agglutination or adhesiveness that holds the infected erythrocytes to the vessel walls. Clinically, the forms encountered are dependent upon the locality in the central nervous system in which occurs the greatest invasion of parasites. Any topographical syndrome may be represented.

Perointzky finds in the cerebrum and cerebellum marked hyperemia of the pia vessels, subarachnoid, perivascular and pericellular spaces and obstruction of the capillaries; their endothelium being swollen with masses of changed red blood cells, which slowly pass through the capillaries, owing to their increase in size and decrease in elasticity, temporarily causing complete thrombosis. These circulatory disturbances lead to punctiform hemorrhages in the gray matter and at the boundary of the white brain substance and necrotic processes in the brain cells.

Weingartner[30] cites a postmortem examination in a soldier, aged twenty-seven years. There were purpuric bleedings in the internal capsule, extensive calcification of vessels with inflammatory foci

of a granulomatous nature, such as were first described by Dürck (malarial granuloma). In the adventitial spaces there were deposits of lipofuscin. These secondary hemorrhages, giving pressure and irritation to the nerve cells until absorbed, assume a place in the pathology of pernicious malaria almost as important as the parasites, pigment or disintegrated red cells, giving rise to thrombosis and embolism. They continue a process begun perchance after the organisms have been removed by quininization. In fact, Laveran believes the alleged polyneuritis of malaria is often really a myelitic hemorrhage softening.

The existence of toxin, the product of the malarial parasite, is almost universally assumed by students of malaria. One argument is the existence of coma in malaria without parasites or pigment in the brain. Ewing[31] says that the majority of cases of comatose malaria coming to autopsy do not show a massing of parasites in the brain. He attributes these cases to general toxemia. However other observers differ.

Deaderick, in discussing pernicious malaria, says that we ought to seek in the conditions of the ground whose quality is so different, and not in the quantity of seed, for the reason which will explain to us gravity of the disease.

Cerebral Malaria with Aphasia. Cerebral malaria having a heavy and more general segregation of parasites in the brain may assume the form of any brain disease, and is frequently found in malarial districts. The estivoautumnal parasite is most often the etiological factor, yet the benign tertian may be the cause of these grave disturbances. To attempt a classification of the cerebral forms would serve no useful purpose in this paper, but emphasis must be placed upon the fact that mental symptoms very frequently accompanying such forms of the disease are not commensurate with the cerebral trauma, due to parasites *per se*. Jones,[32] in discussing one phase of the subject, says violence and irrational behavior are more frequently noticeable in these patients than they are in cases of hemiplegia of the usual hemorrhagic or thrombotic origin. Many interesting cases of cerebral malaria are given in the bibliography.

Of the cerebral manifestations motor aphasia, produced by blocking of the capillaries of Broca's areas by parasites, pigment and other matter for varying periods of time, with occasional secondary effects, such as hemorrhage and softening of the part, is the most interesting and possibly the most rare.

Rao[33] cites a case in a male, aged nineteen years, who suddenly vomited, fell down, became unconscious and was found to have lost his speech upon regaining consciousness. Plasmodium falciparum was found in his blood and after being given quinin by hypodermic injection for three days he regained his speech as suddenly as he had lost it.

The benign tertian parasites may also give rise to this complication as in the case cited by Dee,[34] in which aphasia lasted ten days. Following two days of chills and fever the patient lost his power of speech. Tertian parasites were found in his blood, and under quinin therapy he regained his speech.

Browne-Mason[35] reports a case of malignant tertian malaria complicated with motor aphasia of longer duration than either of the foregoing cases. After suffering fever for four days the patient "became without speech," and while he could not speak, yet he could understand what was said to him when vigorously aroused. Twenty-five days later the patient had regained his speech.

Gillot[36] believes aphasia, isolated or associated with other paralyses, is the most curious, although the most rare of the manifestations of malaria acting on the cerebral centers. Here is a case of motor aphasia he quotes as a complication of tertian fever, of interest because of its short duration: A school teacher, who had just had tertian malaria, suffered cephalic congestion more intense than usual on one occasion. Suddenly it was impossible for her to move her right arm, and she was unable to call out. While she easily recognized her husband, heard and understood his words, it was totally impossible for her to make reply. This hemiplegia with aphemia lasted for three hours. There were no hysterical stigmata present; malaria was the only cause.

Gillot says that it is not impossible to see the aphasia renew itself in intermittent fashion during consecutive attacks. Possibly passing aphasia may be the only manifestation of a larval form of malaria.

Neurological Manifestations. Passing notice may be given to the neurological manifestations of malaria not frequently seen, yet of value to acquaint one further with the action of malarial toxin. The complications may be divided into peripheral, medullary and central.

Of the peripheral complications, we have neuralgias and neuritides. Jones[32] has published his interesting findings on segmental hyperalgesia in malaria, and in brief he found that of 120 cases examined for this sign 70 per cent were positive. Of the 83 cases, this sign was 100 per cent positive in the seventh dorsal area, but varied infrequently above and below this area. Cases of neuritis of malarial origin are numerous in the literature, either simple or multiple in type.

Paralysis of the vagus center in the medulla is the cause of sudden death in malaria and transitory paralyses, such as motor aphasia, are occasionally met with in the literature. Heat stroke, which may and frequently does progress to coma, is reasonably supposed, as Milner points out, to be due to intoxication of the heat-regulating center. He also points out that once this apparatus is upset the body will assume as nearly as possible the temperature of the

atmosphere. Heat stroke does not supervene because sweating ceases, but the patient ceases to perspire because he has got heat-stroke and is suffering from paralysis of the heat-regulating center. In fact, Milner[37] would have us believe that heat stroke, as a clinical entity, is non-existent and that it is nothing more than a symptom of malignant tertian malaria, and in support of this view he gives some admirable observations. Chavigny says that quinin may cause transitory paralysis of medullary origin, and that it is difficult at times to distinguish between the effects of alcohol and syphilis.

Both upper and lower motor neurone paralyses are found in connection with malarial infections. Blin and Kerneis[38] report a case which resembled anterior poliomyelitis in many ways, and, in fact, was regarded as this disease, but was really due to malarial infection of the nerve cells of the anterior horns of the cord. Many cases of monoplegia and hemiplegia of central origin are reported in the literature.

A counterpart for the peripheral neuralgias is found in the usual headache accompanying malarial fever. In some individuals the headache is severe, and as such is a forerunner of coma. Stedman[39] reports a case of malaria in which severe paroxysms of headache were the only symptom. Ettinger also reports 3 cases of malaria in which severe headaches were the most prominent symptom.

That there is a central component comparable to peripheral neuritis seems to be obvious. Manson remarks in his book that loss of memory, partial or complete, appears to be a common accompaniment of peripheral neuritis of malarial origin. Since Korsakow's psychosis is found in cases of alcoholic intoxication showing polyneuritis, a case of Korsakow's psychosis of malarial origin, as described by Carlill,[26] would seem to strengthen the assumption.

Malarial Tremors. Closely associated with neurasthenia, and sometimes a symptom of it, is the malarial tremor, however, the condition has been found by some observers as a separate entity.

De Brun's[40] observations were on cases without the slightest suspicion of alcoholism, neurasthenia, exophthalmic goiter or any other affection capable of producing a tremor. As a general rule, both upper limbs were affected equally; the tremor was not strictly limited to the upper limbs, but other parts of the body are much less affected. He found that intentional movement, prolonged effort or emotion, considerably aggravated the tremor; that the malarial tremor was essentially unstable and frequently underwent rapid changes in its intensity, not only from one day to another, but even in the same day, often without appreciable cause; and finally he believed it to be due to an infectious toxemia.

Jourdran[41] agrees when he says that he has not found the malarial tremors to be a persistent symptom and believes them properly classed as toxic tremors. He also states that the tremor which he observed in a very clear case could not be compared to the

chill which often marks the initial stage of the attack; that it disappeared completely with the cessation of the attack, and that malaria may, like intoxication, give rise to a tremor that should not be confounded with other known forms observed in diverse diseases or disturbances of metabolism. Boinet has published a case of tetaniform tremor of malaria; Lemoine and Chaumer, a Parkinsonian phenomenon; Boinet and Salabert, a malarial chorea. Fornaca[42] reports a case of malarial tremor, not affected by active muscular effort, neither increased nor decreased. The tremor was accentuated with the periodic occurrence of fever and was differentiated from a chill even by the patient himself.

NEURASTHENIA. Neurasthenia accompanying malaria, and conditioned by a low-grade infection over a long period of time with occasional exacerbations, is quite frequently observed.[43] Pope says that in chronic malarial cachexia the nervous symptoms are most marked and neurasthenoid in character. However, all mental and nervous symptoms are less in degree than in the neurasthenia. There is general depression, irritability and nervousness, and a tendency to emotionalism. Numerous somatic complaints, such as vertigo, insomnia and headache, have for their basis vascular disturbances.

Atkinson[44] states that the victim of this postmalarial condition is in a pitiable plight. He is a physical and nervous bankrupt. His defenses are all spent; the very fountain of his sustenance—his hemopoietic function—is vitiated at its springs; he suffers from a dozen inroads upon his debilitated system and is an easy prey to a dozen others. He is frightfully depressed and without ambition.

A very illustrative case is reported by Musgrave[45] in an army officer, aged forty-two years. His initial infection was in Cuba, in 1898, and after that time he had numerous attacks of what later proved to be tertian malaria which finally led up to a neurasthenoid condition. In 1909 the patient thought he was going "insane," complaining of mental and physical debility. He was invalided to the United States from the Philippines with a diagnosis of melancholia and severe cerebral neurasthenia. Authorities at that time recommended his transfer to an insane asylum. He was mentally depressed, tended to be seclusive and complained of photophobia which was marked, especially during an attack, and continued until the real cause was found and treated. At one time the patient was in need of constant attention. Before the cause of his behavior was known the patient was about to be courtmartialed for malingering.

EPILEPSY. Malaria has varying effects upon those predisposed to epilepsy and upon those suffering from the disease. Cases have been called to my attention in this hospital in which the patient attributed to malaria the beginning of his epileptic attacks. These might be disregarded, but facts point to the possibility of there being an element of truth in their statements.

Francis Hare[46] believes there is a well-marked malarial epilepsy, and refers to cases mentioned by Jacobi, Payne, Hamilton and others to the effect that such occur occasionally in the Southern States and in Brazil. "In Hamilton's case a young man, who had lived for many years in an exceedingly malarious region, had more or less periodic epileptic attacks, attended with great preliminary rise of temperature and intense congestion of the face and head. . . Change of the place of habitation and the use of quinin removed the disease entirely."[3] We imagine that the intense cutaneous vasoconstriction, associated with ague paroxysms, may in some circumstances develop so rapidly and widely as to preclude adequate compensation by the muscular vasodilatation of rigor and so lead to vagus inhibition of the heart. This view is, I think, fully recognized by Broadbent, who points out that the cold stage of malarial fever may be carried to such a degree as to bring the heart to a standstill and produce fatal syncope or serious nervous complications.

Epileptic attacks are held to differ from rigors mainly in the nature of the compensation for the extensive vasoconstriction common to both. Trousseau regarded rigor as convulsion minus the cerebral phenomena. The view adopted explains the absence of cerebral phenomena from rigor; muscular vasodilatation anticipates cardiac inhibition: Thus the occurrence of rigor prevents (in a strict sense) the occurrence of convulsions.

So that in those of a neuropathic disposition the vasoconstriction occasioned by a malarial paroxysm may be of such extent as to cause vagus inhibition of the heart which may result in epileptiform convulsions.

Régis[5] states that malaria ameliorates epilepsy at times. This action is rare, although more frequent than in hysteria. It awakens, aggravates and provokes epilepsy. Malarial epilepsy does not present any distinctive character.

Marandon de Montyel,[47] who has done considerable work on the subject, believes, from a series of 14 observations in the course of eleven years, that malarial fever does not lessen attacks in epilepsy. In 5 cases of mild epilepsy, with slight attacks at long intervals and with little mental impairment, the symptoms were aggravated during an intermittent fever which yielded readily to quinin. In 3 cases in which there had been no convulsive seizures for a number of years the attacks returned under the influence of malarial infection. In the remaining 6 epileptic attacks occurred for the first time while the patient was suffering from malarial infection, and in another they were worse under the same condition, although they occurred also independently. In a third epileptic whose attacks developed during a second relapse of malarial fever the attacks recurred, and the patient remained delirious after the malarial fever was cured. The patients in the remaining 3 were

addicted to the use of alcohol, but this was considered merely a predisposing factor in 1 case and the exciting factor in the other 2, the malarial infection operating, however, as an aggravating influence. It should be added that all of the patients possessed a neuropathic disposition.

Hysteria. Hysteria in relation to malaria holds a place quite similar to epilepsy.

Regnault[48] quotes a typical case of hysteria provoked by malaria, and in conclusion states that if the intermittent fever can produce trembling and paralyses, as several cases reported by Bonnet in the *Revue de Médecine* testify, it is only the provoking cause. The effective cause then is hysteria, and one will search for the diverse symptoms of it whenever one sees a case of paralysis or of trembling, even appearing under the direct dependence of an acute infectious malady.

Roux[49] states that it is an actual fact well known that malaria must be counted among the number of provocative agents of hysteria. He is unwilling to say that malaria could be the sole cause of hysteria or whether it merely fosters the development of such a neurosis. His observation on a case that he reports favors the last point of view, and is interesting especially because of the mode of evolution of the neurosis. Manifesting itself at the beginning in a non-convulsive form, which gave to the malarial fever a particular character of perniciousness, it terminated during convalescence with typical crises of convulsive hysteria. These pernicious attacks represented thus an exaggerated mode of reaction of a predisposed organism under the influence of malaria. This reaction was shown by nervous symptoms, which in one patient disclosed hysterical phenomena, and this hysteria, until then latent, manifested itself during the attack of malarial fever. The nervous crises find an explanation in the malarial anemia which "provokes the manifestation of the neurosis in predisposed subjects besides by their personal or hereditary antecedents" (Laveran).

Régis quotes the conclusions of his pupil, Commeleran, on hysteria: "Malaria appears to be susceptible of ameliorating hysteria, but this action is altogether exceptional. It awakens and aggravates a preëxisting hysteria. It provokes the manifestation of the neurosis—most often in predisposed neuropaths and in some cases in subjects who have no morbid antecedent, personal or hereditary. In the first case the neurosis thus provoked offers few special characters. It is especially convulsive, with incomplete crises and hyperesthesia. In the second it seems to particularize itself: (1) By the presence of an hysterogenous zone at the level of the liver or of the spleen, according to the organ which is most often affected by the infection; (2) by the predominance of the hysterical phenomena in the half of the body corresponding to the

hysterogenous organ. It seems that it would be necessary to take account of hysteria in certain pernicious attacks and some of the postmalarial paralyses."

Marandon de Montyel[50] reports 8 cases of hysteria associated with malaria observed over a period of twelve years, and states that there is not malarial hysteria any more than there is malarial epilepsy. For the two malaria is a provoking agent. In 1 case that he reports there was a notable aggravation of benign hysteria twice a year with the return of malaria. In 2 cases hysteria was reawakened by malaria after a quiescent period, 1 so long as eleven years. Discounting the family and personal history as given by the patient, and laying more stress upon his physical and psychic stigmata, we are enabled to see that malaria acts powerfully to provoke hysteria.

As to the time factor, hysteria is aggravated immediately by malaria; to recall a preëxisting neurosis that has disappeared for several years the organism must suffer a greater amount of malarial poisoning; to provoke this neurosis it was often observed to take five, twelve and eighteen years.

Case Reports. In 5 definitely psychotic patients at St. Elizabeth's Hospital I have observed attacks of frank malaria, and in the records have found 7 similar cases. Four of the 12 cases were diagnosed tertian malaria from blood smears, while the remaining number were not typed. Prompt quininization in a few of the cases must be considered as a preventive in the development of psychotic symptoms. The mental examination of these patients was incomplete and amounted to a casual observation of their status, sufficient, however, to assure one that the malarial infection neither ameliorated nor aggravated their mental symptoms, nor added to those already present. However, from the foregoing, the hereditary or acquired nervous and mental imbalance factor in malarial psychoses appears to assume none the less an important role, explained on the following basis. These patients had made a hospital adjustment and were not so easily disturbed by a toxic agent which to one fighting life's battles with an inferior nervous system and personality make-up might have proved the last added force needed to take them out of reality.

The following 3 cases of psychoses associated with malaria have come under my personal observation and have been studied thoroughly:

Case I.—A. B. P., a private in the Marine Corps, a native of Spain, aged nineteen years, well developed, weighing 169 pounds, exhibited no defects on physical examination save a slight mitral leak that was well compensated.

History. Neither organic nor psychiatric determinants were present in the family history. The patient was born in Camillas, Spain, in 1904, the youngest of five. His birth was normal, and he had been breast-fed. He had had no diseases of childhood; he began school at the age of five years and completed the eighth grade at the age of thirteen years. There was nothing of note in his early youth until the age of thirteen years, when, because of punishment in school, he left home. It seems as though his strongest urge was nomadism, for from this time on he worked as kitchen boy on transatlantic liners. He held many jobs, always doing his work well, but he was inclined to give up and "rest awhile," as he expressed it. During these rest periods, which occurred every six or seven months, most of his earnings were spent in gratifying his sexual desires. He had his first heterosexual experience when fourteen years of age, and continued at regular intervals, but denied homosexual practices.

He joined the Marine Corps in 1920 to become an American citizen. He drank excessively at times, but never had delirium tremens. From his service record the following was abstracted: At Slato-Mayor, late in the summer of 1921, the patient had a light attack of influenza and tropical lymphadenitis; at San Pedro de Macoris he had dysentery (unclassified). In December of the same year malaria was diagnosed from the blood (type not given). The patient had a chill with a temperature of 104°, and was treated with quinin (15 gr. three times a day); he was returned to duty, December 31, 1921, with orders for continued quinin treatment.

From the patient's own story he must have lost his mind at that time, for he remembered nothing from January, 1922, until June 14, 1922, when he was admitted to St. Elizabeth's Hospital and was told the date and where he was. His service record, dated April 21, 1922, gave the diagnosis psychosis, unclassified. The patient was in confinement for several months, and talked irrationally. He was disoriented in all fields, did not know his name, was very restless, but apparently in good physical condition.

His record states as follows:

April 22, 1922: Insomnia; refuses food; destructive to clothing; yells and sings continuously.

April 23: Becoming more violent; restrained.

April 24: Attacked the guard.

May 1: No improvement.

May 8: Not quite so active; Wassermann negative.

May 7: No improvement; some days he is quiet and sullen; others, very noisy and hilarious; not destructive to clothing.

May 20: Subject to moody spells; no evidence of violence for some time.

May 27: Transferred to the States; caused no trouble except when he saw a negro. This seemed to enrage him and he would attempt to strike the negro. Sleeps and eats well. Vocabulary increasing. Seclusive.

At the United States Naval Hospital, Norfolk, Va., the patient's psychosis was unclassified. The patient was mute, restless, destructive, smiled at examiner and answered "chow;" made his desires known by signs; was greatly excited at the sight of a negro, but quiet at other times; apparently reacting to hallucinations and delusions.

June 7: Quiet, mute, completely disoriented.

June 14: Upon admission to the United States Naval Hospital, Washington, D. C., the patient was inaccessible, out of touch with his environment and repeated "chow poo" frequently; emotionally unstable, introverted and seclusive. Stated he hated negroes and would kill them.

Late the same day he was transferred to St. Elizabeth's Hospital, where he complied with routine procedures. When interviewed he was found totally disoriented; he though he was in Santo Domingo and that it was January, 1922. When told the name of the city he was in, the month, and so forth, he evinced great surprise and wanted to know where he had been for the past six months. He remembered being placed on the sick list, December 23, 1921, suffering from malaria. His head was "big" and he had fever; he was returned to duty, and about January 5, 1922, vaguely remembers being sent to a hospital, but that is all. When questioned about negroes he gave out some paranoid ideas regarding them and explained that the reason why he had more trouble with them than the other marines was because he, speaking Spanish, could understand their speech and resented their referring to the marines in derogatory terms.

June 21: Blood Wassermann test and routine urinalysis was negative.

June 29: Blood analysis: Hemoglobin, 80 per cent; erythrocytes, 4,720,000; leukocytes, 7240; polymorphonuclears, 33 per cent; lymphocytes, 64 per cent; eosinophiles, 3 per cent. No malaria organisms were present.

During his stay on the admission service he accused a nurse of having his sombrero (which he never had), and on July 1 he was observed to be somewhat disturbed and apprehensive; he had little to say and expressed the idea that he was to be returned to San Domingo. It was brought out that this occurred to him when he saw two marines who came to the hospital for some personal effects of a former patient.

On August 2, 1922, mental examination brought out nothing psychotic save a period of amnesia lasting from January, 1922, until June, 1922. The patient was granted ground parole, August

18; he abused none of his privileges, and, due to his dependability and thrift, was granted city parole, September 22.

The patient has been adjusting well; he is bright and cheerful, and keeps occupied during the day; he wishes his discharge, so that he may get a job on a transatlantic liner before winter sets in.

This is a case of psychosis in a male adult in which malaria seems to have been the chief factor. No hereditary determinants present themselves. Nomadism and a tendency to excessive drinking are factors which might well indicate a somewhat unstable make-up. The former fault exhibited itself in boyhood, and the latter seems to be not deeply rooted. The patient explained that the natives were afraid of the marines, so that frequently they would go to a native store, getting all the liquor they desired on demand. As he reviewed these happenings, he gave the impression that he had indulged in a youthful prank, and was not a seasoned drinker.

Now that this patient has cleared up entirely, he gives the impression of being of quite a stable make-up. As regards stressful circumstances, these seem to be lacking, for he was well liked by his equals and superiors. He made friends with those of his own rank, and enjoyed being in their company. In fact, he was of special value to his commanding officer, because of his knowledge of Spanish. Alcoholism was certainly a factor, together with his malarial infection, and the combined effect has been observed to bring on just such a mental upset as this patient exhibited. His confusion, hallucinosis and amnesia are typical, save that his amnesia was over a period much longer than any cases found in the literature.

CASE II.—E. M., an adult white male, aged thirty-four years, weighing 156 pounds, developed mental symptoms following an attack of malaria in November, 1921. Physical examination revealed nothing abnormal, and he was in a fair state of nutrition. The blood Wassermann test was negative, and urinalysis showed a few hyaline casts, but was negative for sugar or albumin.

No psychopathic determinants were elicited in his family history, and his family life was free from mental conflicts. As a child he was puny, pale and anemic, and because of his poor health he was kept from school until late in his second decade. His attendance at school was intermittent, and he never went continuously for more than five months; he left school when twenty-one years of age, having completed the third grade. He seems to have made a good economic adjustment, working on a farm until drafted into the army in 1918, where he served until after the armistice. Not being satisfied with farm life after his sojourn overseas, he enlisted in the Marines in April, 1921. He was sent to Haiti, contracted malaria on November 20, 1921, and before full convalescence he began to show mental symptoms, the most prominent of which was

marked depression. The patient stated that he had always been a heavy drinker since childhood, and that he could drink a large quantity of whisky a day.

On March 17, 1922, the diagnosis was made of dementia precox, and March 31 he was transferred to the United States Naval Hospital at Norfolk, Va. Admitted on April 13, he was fully oriented, easily confused, disinterested in things about him, and would remain in one position for hours at a time. No hallucinations or delusions were elicited at that time.

On April 24 he was transferred to the United States Naval Hospital, Washington, D. C., where he was noticed to be greatly retarded, introverted and almost inaccessible, mildly catatonic, depressed and apparently was reacting to delusions. At the hospital he suffered a relapse of malaria (due to Plasmodium vivax). He acted peculiarly; entertained persecutory ideas and tried to escape; became disoriented and apathetic; was deteriorated and exhibited mild cera flexibilitas (waxy flexibility). He was markedly retarded, disinterested, and only talked when questioned; he denied hallucinations at that time.

On April 26 he was admitted to St. Elizabeth's Hospital in the same condition. He said he thought there was something wrong with his head, and had a dizzy feeling at night. Things appeared before his eyes at night—animals, "varmints," faces of his kinsfolk; he had auditory hallucinations of his mother's and other people's voices. At times the voices called him bad names; he seldom was hallucinated in the daytime, and was not positive of persecutory ideas.

Upon entering the examination room, May 18, the patient presented an unkempt, untidy appearance. He walked in a listless, languid manner; was coöperative, but quiet and introspective; he showed psychomotor retardation, and approached the condition of catatonia. He was confused during the examination; had slight insight and his judgment was defective. Memory for recent and remote events was poor and numerous other mental tests showed him to be defective. Visual and auditory hallucinations of his kinsfolk were present; paranoid ideas were lacking, and he was disoriented in all fields.

On June 1 the patient appeared fairly well nourished; he was in a state of agitated depression; picked at his clothing continuously and admitted auditory hallucinations. He spoke in monotones in a meagre somewhat irrelevant manner; he was untidy in his appearance.

On July 14 the patient had a frank chill, following which his temperature rose to 106°. Quinin treatment was instituted immediately, consisting of 45 gr. a day for one week, and 15 gr. a day for a week thereafter. At 8 o'clock the following morning the patient's temperature was normal and has remained so since that

time. The urinalysis was negative. The blood count showed: Erythrocytes, 3,130,000; leukocytes, 6000; polymorphonuclears, 79 per cent; lymphocytes, 21 per cent; large numbers of Plasmodium vivax.

Hyperpyrexia and quinin therapy did not aggravate his mental symptoms.

When examined, July 26, the patient stated he felt very much better. He was correctly oriented; his speech was retarded and monosyllabic. He was somewhat apathetic, and referred to having heard voices in the past, but denied them at present; he had slight insight. On August 26 his blood was entirely normal; no parasites were found.

On September 22 it was noted that the patient had made slow improvement, which began soon after quinin therapy was instituted. While he was still retarded he took more interest in his surroundings, paid better attention to his personal appearance, was correctly oriented, and stated that he felt very much better. No definite delusions and hallucinations were elicited.

Physically he appeared somewhat undernourished.

Undoubtedly this patient had a strong predetermining factor, as shown in his early backwardness physically and mentally, his addiction to alcohol and his failure to readjust to his former occupation and his desire to wander about. Nevertheless, it seems from the history of the case that one must attribute to his malarial toxic infection the additional factor in the development of his psychosis. He did not react to this toxic condition by delirium and acute hallucinosis, as is noted in some cases; but very likely his psychosis took the path of least resistance and showed itself in catatonia. That he improved slightly after his first treatment with quinin is evident. However, a relapse of malaria brought on an aggravation of his mental symptoms, and with quininization for the second time he again showed mental improvement. Whether he ever entirely recovers is doubtful, and he may be well classified a case of dementia precox; however, it is obvious that malaria had more than a casual relation to his psychotic manifestations.

Case III.—A. B., a retired army sergeant, aged fifty-three years, but in appearance much older, in a poor state of nourishment, quite cachectic, was admitted to St. Elizabeth's Hospital, August 10, 1922. His family history was negative for psychiatric determinants; also his personal history was negative until he entered the army at the age of twenty-one years. He says he enjoyed army life; he was courtmartialed three times for being absent without leave and for "booze fights" during his long army career. He drank moderately all his life, but very occasionally became intoxicated.

While in Cuba, in 1898, he contracted malaria, and was sick for

three weeks, but had no mental symptoms. Since that time he has lived without chills for several years at a time, but in general was able to predict the onset of chills every fall. In 1903, during a relapse, he became erratic for a short time during the febrile period.

In October, 1921, the patient, while at Letterman General Hospital, was diagnosed as a case of psychoneurotic hysteria, from which state he recovered and was discharged, November 8, 1921.

After suffering chills and fever for a week the patient was readmitted to the same hospital. Examination at that time found him very much undernourished; all superficial lymph nodes were enlarged; arteriosclerosis was present; his blood-pressure was 180/140 mm.; his spleen and liver were enlarged. The patient comprehended questions poorly, and had a poverty of thought. Occasionally he was restless and agitated; he had changeable delusions and mild auditory and visual hallucinations. He was confused and disoriented as to person, with marked fabrications of memory. The blood Wassermann test and neurological examinations were negative.

The patient was quite confused when admitted to St. Elizabeth's Hospital, and did not know why he was sent to such an institution unless because of confusional states. On August 15 he was found fairly well oriented with slight clouding of memory; retarded in speech and action; emotionally somewhat depressed. His insight and judgment were very good, and aside from occasional confusional periods he seemed quite normal mentally. Physically, he was very anemic; had a cachectic appearance; his spleen was enlarged, and his heart enlarged to the right with a presystolic murmur, heard at the apex. Urinalysis and blood Wassermann test were negative, as was his blood for malarial parasites.

When interviewed, August 24, he was found to be readily made nervous; in fact, ordinary conversation or taking his blood-pressure was sufficient. While in bed he exhibited a very marked tremor in his voice, also in both arms and hands, and even in his neck muscles. He gave the impression of being run down, both mentally and physically. The blood count bears this out: Erythrocytes, 2,170,000; leukocytes, 5600; polymorphonuclears, 21 per cent; lymphocytes, 78 per cent; transitionals, 1 per cent; no malarial parasites present. Urinalysis was negative. Roentgen-ray on August 26 showed the spleen to be moderately enlarged. There had been a low-grade fever (100.4° F.), with remissions. A second blood count on September 6, after the patient had received general supporting treatment, Blaud's pills and quinin, showed: Erythrocytes, 2,880,000; leukocytes, 4600; polymorphonuclears, 25 per cent; lymphocytes, 70 per cent; monocytes, 3 per cent; eosinophiles, 2 per cent; no malarial parasites.

The patient, when examined, September 27, 1922, said that at

times his mind would go blank following a chill. Although he still suffered physically from his chills, his mind now seemed to bear the brunt of the attack. A fear reaction came over him at the time of a chill, and he wished himself in bed, where he knew he would be safe. Said he felt weaker than ever before, and feared lest he should lose his mind. At this point the patient showed considerable emotional effect; he became lachrymose, and with this his tremor became very pronounced. He said that if he had a chill early in the evening he found himself very confused that night, troubled with mild visual and auditory hallucinations. His consciousness seemed to be clouded, as he was retarded mentally and disoriented spacially. His memory was poor. He knew that for the last eighteen months he had had relapses of malaria more frequently and that he had been more confused. His stream of talk was free, relevant and coherent.

There was a gradual decline of his physical condition, with death on October 8, 1922. Autopsy, seven hours postmortem, revealed double bronchopneumonia with double pulmonary edema, acute cerebral anemia, general anemia, hypertrophic hepatic cirrhosis, chronic parenchymatous nephritis and chronic atrophic gastritis.

This case was a classical chronic malarial cachexia brought on by early infection, with frequent relapses. Alcohol played an important role, accompanied by malarial toxins. That he should have been diagnosed as a case of psychoneurotic hysteria seems to have been not far wrong, but does not give any information as to the possible cause of such a psychosis. His tremor and emotional instability are in keeping with chronic malarial cases, due either to a neurasthenic or hysterical development.

The following cases have been abstracted from the hospital records. The first is a case of cerebral malaria, with an autopsy report.

CASE IV.—C. C., aged thirty-four years, was admitted to St. Elizabeth's Hospital from the army, April 21, 1875, with no record of a routine physical examination being done at that time. No family history was available; mental diagnosis, chronic dementia for one year and six months' duration. On October 7 the patient had a chill and was confined to bed, but got up four days later. No diagnosis mentioned or kind of treatment. In December of the same year note states that the patient was up, assisting with the ward work; was quiet and orderly.

No further notes are found until May 1, 1900. At this time the patient was able to walk about, was quiet, rather seclusive, clean in his habits and assisted with ward work. In August, 1900, the patient was put to bed suffering from a chill. He received "ague

mixture" until August 9, at which time the patient felt very comfortable.

Again on September 11, 1902, the patient's temperature reached 102.4° with pulse and respiration in proportion. A laboratory report was positive for estivoautumnal malaria, September 10, 1902. He received "ague mixture" for four days, at which time his temperature remained normal, and he got up and dressed. In October of the same year the patient's mental notes show no change in his condition.

In March, 1903, a note states that the patient was quiet and orderly and helped with ward work; he was seclusive, and of a moodish disposition; physical condition was very good.

In April, 1904, the patient was quite eccentric, remained mute unless spoken to, and spoke in a whisper, but assisted with ward work. No change was noted in 1905 or 1906. In 1907 his habits were fairly tidy; he assisted with light ward work, and seldom complained. In 1908 he showed no change. On January 24, 1909, the patient was very quiet; he remained mute, unless spoken to, and then answered in a whisper; he was fond of reading, and took some interest in his surroundings; psychomotor retardation.

In 1910 the patient enjoyed walking about the lawn; his health was good. December 20, 1910, urinalysis showed very few hyaline casts. There was no change in 1911 until May 15, when the patient had a chill (temperature, 100.4°; pulse, 106; respirations, 24), with remissions continued for three days, reaching its height, 103°, on May 17. He received quinin, 5 gr., every six hours. On May 18 the patient showed psychomotor retardation; hallucinations did not seem to be present; the examiner was unable to learn of delusions since the patient would not talk. Urinalysis on May 22, 1911, was negative.

On June 1, 1911, the patient was quite seclusive, introverted, neat and tidy. On October 7 the patient had a recurrence of malaria; he was put to bed, but was able to be up again on October 10.

November 9 the patient was quite sick; he had edematous ankles, with a rise of temperature and anorexia. He seemed to have little use of his muscles; the temperature rose to 104.4°. On November 12 it came down to normal, returning to 103° at the time of death.

Summary of autopsy report: The brain showed the basilar vessels were slightly sclerotic. The whole brain was hard. On section the gray matter of the cortex and central ganglia was congested. No softenings or gross lesions were found. The heart was normal. The lungs showed hypostatic congestion. There was fatty infiltration of the liver and chronic diffuse nephritis. The spleen was enlarged; the pulp was soft and jelly-like and gray-reddish in color (malarial spleen).

Microscopically there was neurophagia of a few ganglia cells. Hyperplasia of neuroglia tissue was very marked. The vessels

were dilated and congested, and filled with malarial parasites. These were confined to the interior of the bloodvessels; the lymphatic spaces were not infiltrated.

Clinical diagnosis: Undifferentiated psychosis (dementia); cerebral arteriosclerosis.

Anatomical diagnosis: Cerebral arteriosclerosis and malaria of the vessels of the brain.

This patient evidently suffered from malaria for some time before admission, and was continually fighting malarial toxins which were at times made manifest by objective symptoms. His mental examination was meager; however, he was an institutional case suffering from a malignant psychosis which did not show rapid regression. Mental notes unfortunately are not complete, especially during the relapses of malaria. Nevertheless, from his autopsy report we may be sure that additional symptoms must have been present. However, it must be borne in mind that definitely psychotic patients having made a hospital adjustment do not show the characteristic mental reaction to malarial toxins that normal individuals of sound mind may.

While the brain was hardened throughout by an increase of neuroglia, still it is interesting to note that neurophagia took place in only a few cells. Evidently the nerve cells were not destroyed by the toxins, but rather suffered an intoxication therefrom. Cases of cerebral malaria that have come to autopsy are rare in the literature, although it is rather common to see cerebral malaria in highly malarious districts.

Case V showed the typical delirium, confusion and amnesia of a malarial toxic psychosis.

Case V.—L. N., a white adult male, aged twenty-six years, with negative family history, was admitted, June 21, 1909. The patient had a common school education; had a normal earning capacity for one of his education; drank beer very moderately; denied venereal disease; always had a quiet reserved disposition.

He enlisted in the army and was sent to the Philippines, where he suffered his first attack of malaria in July, 1908. He was hospitalized from this time on. In November, 1908, the patient had delusions of persecution, acted irrationally and was melancholic. In January, 1909, he suffered greatly from malaria. Complete mental symptoms are not given in his history, although it was stated that he had "delirious symptoms." However, an amnesic period, while at the Manila Hospital in January, 1909, seems to have a marked psychotic symptom. The patient recalls only the ice baths, indicating that he must have been at that time much confused.

In February, 1909, he was transferred to Presidio Hospital,

California, and after one recurrence of fever and mental symptoms remained free from further attacks.

When admitted to St. Elizabeth's Hospital on June 21, 1909, examination brought out the following facts: Physically, the superficial lymph nodes were enlarged; there was increased splenic and liver dulness; weight was 154 pounds; height, 5 feet 7½ inches, well proportioned. Blood examination was not done, and the urine was negative. Mentally he is neat and tidy, and spends most of his time reading; is correctly oriented in all spheres; seems somewhat depressed; has good insight. From the patient's denial of hallucinations and delusions and irrational acts, it is very evident that he suffered from amnesia for a rather indefinite period of time, during which his malarial symptoms were at their height.

From the nurses' notes taken at frequent intervals during his stay at St. Elizabeth's Hospital, no psychotic symptoms can be gathered.

On November 12, 1909, he was entirely recovered. He recalled being mentally disturbed, but could not recall much that had gone on while he was at Manila. His trip across the Pacific was clear to him. On November 26, 1909, the patient was discharged as having recovered from his chronic malarial toxemia.

This patient from his history showed, notwithstanding the chronicity of the infection and amenability to treatment, quite the typical cerebral accompaniments, confusion and amnesia. Recurrence of mental symptoms bore a direct relation to a relapse of malaria with consequent liberation of toxins.

Case VI exhibits delirium, somatic delusions referable to the gastro-intestinal tract and amnesia, more or less complete.

Case VI.—G. P. F., a white male adult, aged thirty-nine years, married, was admitted, September 30, 1913. He was very much depressed and somewhat mute.

The patient's family history was negative for nervous or mental diseases or alcoholism. His school and economic adjustments were normal. Due to the infidelity of his wife, he separated from her after ten years of rather pleasant married life.

About six weeks before admission to St. Elizabeth's Hospital he had an attack of malaria. He was ill for about two weeks. Following this he became delirious, excited and would not remain in bed. His admission note in September states that the patient was very dull and disinterested in routine procedures; lacked insight; was only approximately oriented; refused to eat his breakfast, saying the food was not good enough for him; he appeared restless at times, and wandered aimlessly about the ward.

Physically the patient was well developed and well nourished. The only positive finding was an area of tenderness localized in the extreme left hypochondrium.

On October 4, 1913, the patient said the reason why he could not eat was because he was constipated, but he refused to take a laxative. On October 7, 1913, the patient was only approximately oriented; he was emotionally flattened; his insight was very poor. He had delusions of persecution; he thought his food had human flesh in it; his memory was poor for remote and recent events. Numerous other mental tests showed him to be in very poor mental condition.

On October 9, 1913, after being transferred to another ward, he showed slight improvement. He was well oriented for time and person; was retarded in thought; he denied hallucinations and delusions; continually found fault.

On October 24 he again had delusions prohibiting him from eating; he had to be tube-fed until November 15; on November 18 he was quite confused.

On December 10 he had delusions regarding his bowels; was negativistic; tube-fed until January 31, 1917. At this time he began to take interest in his surroundings, worked a little, but was still delusional.

On February 17, 1914, the patient was coöperative, but still delusional. On March 4, 1914, the patient was quiet, agreeable and coöperative, and seemed to have improved greatly.

The urine and Wassermann reports were negative, and, although no blood examination for malarial parasites was done at the hospital we may accept the patient's account of his illness. On March 10, 1914, he states that he remembered having chills every other day, felt very sick and must have suffered about a week, during which time he took about 20 gr. of quinin a day. Since that time he cannot recall all the events that transpired. He admitted having persecutory ideas. He said he stopped using alcohol six months prior to his sickness. The patient has a partial amnesia for events that happened during his illness. At the time of this interview the patient was correctly oriented, denied hallucinations and delusions, and was in good physical condition.

The patient was discharged on April 27, 1914, as recovered.

The history of this case seems to exclude a dementia precox make-up, and from the age of onset makes a true precox psychosis doubtful. He evinced almost a complete amnesia from the time of onset of malaria until recovery from his psychosis. His delirious excited period was of shorter duration than some of the cases cited; however, his psychosis seems very closely allied to the attack of malaria, and whether or not malaria was the sole cause of the entire psychosis, at least it seems to have been the final factor.

Case VII has for its initial psychopathy confusion, amnesia, more or less complete, and the possibility of its being an early manifestation of paresis.

CASE VII.—C. E. B., a gunner's mate, first class, United States Navy, colored, aged thirty-two years, was admitted to St. Elizabeth's Hospital on October 9, 1908. His maternal grandfather died insane following sunstroke; his father used alcohol moderately. No other psychiatric determinants were present.

The patient had had the usual diseases of childhood; there was nothing of note in his early youth. He served twenty years in the navy, making good progress. He states that in 1890 he contracted malaria, and since that time he has had malaria every autumn. In 1895 he had two chancres, but no other symptoms from the infection.

In 1907 the patient had several attacks of malarial fever of short duration. About August, 1908, aboard ship, the patient acted in such a way that numerous complaints were carried to the surgeon. Finally he became morose, took no interest in his duties and wandered about the ship in a listless manner. His blood was negative for malarial parasites. He was transferred to the Norfolk Naval Hospital, September 15, 1908, where he was found totally disoriented, mute and seclusive. On September 16 the patient had a temperature of 102° F. Blood examination showed malarial parasites, and quinin (10 gr. every four hours) was given. The patient had a retrospective falsification of memory. The symptoms remained the same throughout the month of September. On October 6, 1908, his temperature was normal. He showed little improvement mentally, was disoriented; had hallucinations of alligators and people dressed in fancy costumes; did not remember how or when he came to the hospital. The patient states that he came to himself after being in the Norfolk Hospital for some time.

Physically, when admitted to St. Elizabeth's Hospital, October 9, 1908, he weighed 148 pounds, his height was 5 feet 8 inches and he was fairly well nourished. His muscles were somewhat flabby, and he had a well-marked stomatitis. There were no nervous symptoms other than slight tremor of the extended fingers.

On October 13, 1908, the patient appeared apathetic and confused. His consciousness was clouded and he was imperfectly oriented in all spheres. His attention was held with difficulty, and his memory for recent events was poor. There was almost a complete amnesia for what happened from the time of his transfer from the Idaho to the Naval Hospital at Norfolk until he was transferred here. Delusions and hallucinations were present at the Naval Hospital, but he denies their presence now. Reasoning and judgment were impaired. He lacked insight. At this time, while taking quinin, the patient had frontal headaches and insomnia, slight rise in temperature and bodies doubtfully resembling plasmodia in his blood. Urinalysis was negative. On October 30, 1908, his mental condition had improved very much. He was oriented in most respects; comprehended questions and his replies were fairly

prompt, coherent and relevant. There was still an amnesia for most of what occurred at the Naval Hospital. Since his arrival here he has been free from hallucinations and no delusions could be detected. Shortly after admission he began to take an interest in his environment, headaches disappeared and the patient gained weight.

On November 28, 1908, he continued to improve and had ground parole. December 31, 1908, the patient showed no evidence of mental disorder but still lacked insight. Diplopia formerly present had disappeared.

On February 3, 1909, the patient was given the privilege of a short visit. The patient got along well and was discharged on August 10, 1909, as recovered.

Although general paresis cannot be entirely ruled out in this case, still we have no laboratory findings indicative of that disease (White). While on the other hand, his malarial infection and recovery seem to bear a very direct relation to the onset of and the recovery from mental symptoms, this patient's history for the following ten years might have brought out more exact knowledge of his psychosis.

It appears that we have to deal with a normal adult negro who contracted malaria many years ago; suffered from numerous attacks, but in 1908 he developed a condition resembling dementia precox, and closely associated with a relapse of malaria probably more severe than usual. Associated with this attack was a very definite amnesia which lifted after quinin medication. Mention was made of diplopia which cleared up with the treatment. This seems to indicate that the toxic infection found the central nervous system a point of attack, and it seems not unreasonable that it could also account for the mental symptoms elicited. Paresis also must be borne in mind.

If the observations of Wagner-Jauregg[51] and others[52] upon the therapeutic effect of malarial toxic infection in paresis are of value, then it may have been fortunate for this patient who may have had paresis to have malaria added to this infection.

Symptomatology in General. The symptomatology of necessity must be varied, and in addition it is of great value to know the patient himself. This can be clearly seen from a review of the literature of the subject; one observer finds depression, another maniac outbreaks, others a short-lived delirium and so forth. The determining factor, to a large extent, is then the individual reaction of the patient.

The patient is confused and is oriented, and at this time shows a tendency to his individual reaction type, a precox form, a catatonis or maniac form and so forth. (Torquato Tasso was considered a subject of malarial melancholia.) A fear reaction appears to be fundamental in all cases.

Due to a lack of attention during the delirium, or rather because of a dissipated attention, the patient awakes from his delirium or confusional state with an amnesia for all that has happened. Complete amnesia is not found in all cases, but in all cases there is at least some impairment of memory. Since the amnesia is conditioned by delirium, it is dependent upon the depth of delirium for its completeness. In chronic malaria the mental picture, while less distinct, is fundamentally on the same basis as in the acute outbreaks. At times a reaction similar to the acute psychosis is seen, but most frequently there results a malarial neurasthenia. The psychosis often acts as a malarial equivalent, and in this case an ephemeral mental confusion takes the place of an attack; that is to say, there may not be an appreciable rise in temperature nor the usual signs of an attack, but instead a short-lived mental confusion may represent the entire symptomatic picture. These short attacks of mental confusion can hardly be designated a psychosis, but when occurring frequently so incapacitate the patient that they approach that of a true psychosis.

Summary and Conclusions. That there is a malarial psychosis can be definitely stated, but on account of many factors, its physiognomy is of necessity varied.

Of the determinants giving a diverse mental picture may be mentioned: Alcohol, severity of the attack *per se*, age of the patient at the onset of the malarial attack, even the acuteness or chronicity of the disease, and lastly, hereditary taint. A few manifestations, however, are quite constant, such as initial mental confusion, oniric delirium and more or less complete delirium.

The symptoms of a malarial intoxication with its oniric delirium resemble those of other toxic infectious psychoses. They are modified somewhat by hepatorenal insufficiency.

Although patients with a malarial psychosis are frequently found to have been alcoholic at the time of onset of the disease, and although malarial patients are capable of easy alcoholization, alcoholism has not been found to be a necessary accompaniment.

Arabs, who were not as a class alcoholic, whenever they developed a malarial psychosis, lacked the initial delirium, while Europeans with an alcoholic taint, on the contrary, always developed an initial delirium. This is so constant that several observers have taken it as an indication of alcoholism.

The severity of the malarial attack in a susceptible individual is on a quantitative basis, and so determines his reaction. With a florid attack the quantity of malarial toxin is greatly in excess of that of a mild attack, so that in the former case we would expect greater mental aberrations than in the latter.

Depression has been most frequently observed in children.

Jews as a race tend to develop a catatonic reaction.

The mental symptoms appearing with the first infection of

malaria are generally: (1) Delirium, which is intermittent, not very well sustained, rather monotonous and not expansive; (2) confusion with dream delirium, followed by amnesia dating from the onset of delirium and varying in its completeness.

In chronic malaria the individual attacks are less severe, less noticeable, generally taking the nature of a depressed mental state, and gradually shading into a neurasthenic or hysteroneurotic condition.

A nervous system with hereditary taint is suitable soil for the development of a malarial psychosis. This and the malarial toxinfection are in themselves capable of setting up mental aberrations in a patient, but probably as often as not alcoholism is also present. This in turn aids the malarial intoxication and results in a mental upset.

Twelve cases of malaria in patients suffering from several different types of psychoses (non-organic) did not show added psychotic symptoms. The failure to elicit mental phenomena due to malarial intoxication, however, does not detract from the hereditary factor in malarial psychoses. Old hospital cases on "back wards," not subject to the careful scrutiny and study that newer and more hopeful cases demand, might easily develop some few new mental symptoms under a malarial attack and have these overlooked. Again, in non-organic cases already on a low mental level, living the well-protected life of an institution, malarial infection might conceivably be insufficient to bring out aberrant mental reactions, such reactions as might be termed significant of a higher mental state bearing the brunt of a toxic infection.

In one case herewith reported, paresis could not be definitely ruled out, although the tendency was to believe that his mental upset was due to malaria. In this connection it is interesting to note that Pilcz,[53] using von Wagner's treatment for general paralysis, occasionally noticed acoustic hallucinations, ideas of persecution, delirious and catatonic states in those subjects infected with malaria. All their symptoms disappeared when quinin was given.

Pathologically, of outstanding importance is the plugging of small arterioles and capillaries in the brain and spinal cord. The thrombosis or embolism in perforating arterioles, if not fatal, causes the most serious consequences. This tendency to thrombosis and embolism partly explains the presence of almost any of the topographical neurological syndromes noted occasionally in the course of malaria. Most interesting, as well as most rare, is the development of motor aphasia, due to the blocking of capillaries surrounding Broca's area.

The delirium is well explained by the marked hyperemia of the pia vessels, subarachnoid perivascular and pericellular spaces, and plugging leading to punctiform hemorrhages.

The development of coma is found to be due, aside from such preëxisting conditions as anemia, cachexia, physical or mental fatigue, the puerperium, insolation and alcoholism, to the number of parasites present, the amount of toxin secreted and, most of all, to localization of the toxi-infection in the brain.

In cerebral malaria the symptoms may simulate any brain disease, but the mental symptoms are not commensurate with the cerebral trauma due to the parasites *per se*. They are exaggerated, and point to a cerebral intoxication.

Neuritides, neuralgias, hyperalgesia, headaches, and acute hyperpyrexial attacks are but indications of the effect of malarial toxins on peripheral and central neurones.

Amnesia of malarial origin is conditioned by the lack of attention during and after the initial delirium, and is of varying grades. One case studied had an amnesia for six months.

As aforementioned there is a difference of opinion on the exact clinical picture exhibited in a malarial psychosis. From the first there is a bradypsychia which observers have found to progress to a frank depression. Maniacal outbreaks, not frequently observed, can only be attributed to a constitutional predisposition. Depression is always noted in varying degrees in those long affected with a malarial infection. One writer explained this from the fact that most of his cases of malarial psychosis were in women, and they are the more given to depression. Racially speaking, Jews, when affected with malaria, have been found prone to a catatonic development. Several observers have noted that the malarial mental confusion has, for its essential character, the accompaniment of certain symptoms which evolve toward dementia precox catatonia. In my first case of malarial psychosis it was the consensus of opinion that the patient was a case of catatonic dementia precox. Each consultant, however, expressed some doubt as to the diagnosis, and was wont to give malaria as the possible cause of the development of the psychosis.

Malaria over a period of years, with a history of rather frequent outbreaks, is capable of bringing on a marked neurasthenic condition. Aside from the possible psychic effect of a chronic debilitating infection, malaria attacks the hemopoietic function and vitiates it at its source, thus making the patient a fit subject for neurasthenia.

Epilepsy and hysteria, according to good observers, are caused by malaria, and in preëxisting conditions the infection serves to aggravate the symptoms of both.

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THE RELATION OF FUNGI IMPERFECTI TO DIARRHEAL CONDITIONS.

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and

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About two years ago we became interested in the problem of the occurrence of fungi* in the intestinal canal of human beings, and began a study of the stools of normal persons, as well as those of persons in hospitals, for condition other than gastrointestinal disturbances. However, we were soon led to an interest in cases

* We use the terms fungi imperfecti, oöspora, monilia, monilia-like organisms and common yeasts throughout our article in a somewhat loose sense, since we have as yet not definitely placed many of the organisms isolated, and since we are as yet undetermined as to which of the numerous botanical or medical classifications to follow. However, when we speak of common yeasts we refer to organisms showing a yeast-like form which would be classed as ascomycetes (having an ascospore sac), and especially organisms which fall outside the group of fungi imperfecti. By fungi imperfecti we mean organisms which do not belong either among the ascomycetes or phycomycetes, and in which reduction takes place by means of conidia produced on conidiophores which are either enclosed in perithecia placed on disks or are unprotected. The oöspora, monilia and monilia-like organisms, we believe, all belong to the family Oösporaceæ, Saccardo 1886, and show septate hyphæ; conidia are produced on simple carriers and conidia appear in rows. In the ones we have called oöspora there is a tendency for the hyphæ to break up into the conidia. The monilia show a tendency to produce conidia at the ends of the hyphæ, which do not break up as in the case of the oöspora, and there is a tendency toward the appearance of the conidia in clusters. The monilia-like organisms are very similar to the monilia, but show certain minor differences.

in which there was evidence of intestinal disturbance, and we have now for some time been studying cases in which there existed a chronic diarrhea. Our studies have not lead to positive conclusions, but so much material has been collected that we cannot escape the belief that a relationship exists between certain types of fungi imperfecti and some diarrheal conditions. We publish this article, therefore, with the hope that further studies may be made in this direction, and that with the accumulation of evidence this relationship may be more sharply defined.

Fungi have been considered by a number of individuals to be the causative agent of specific intestinal disturbances, and in the past ten years or so this relationship has been especially stressed in connection with tropical sprue. We shall not attempt to review here the literature concerning the etiology of this disease, because it has recently been fully covered in an article by Bastedo and Famulener.[1] Suffice it to state that Ashford,[2] investigating a large number of cases of sprue in Porto Rico, came to the conclusion that a specific organism, to which he gave the name Monilia psilosis, was the causative agent. Many observers, especially Castellani,[3] do not agree with his conclusions. However, in recent years Castellani[4] has somewhat modified his position, and in a more recent publication states that, while he cannot definitely deny the possibility that fungi imperfecti may have something to do with sprue, he does not believe the Monilia psilosis of Ashford to be the only organism which might be associated with sprue. Also, that if fungi imperfecti are concerned in this disease there are several different varieties which may possibly be causative agents. Of such, he mentions about seven species of both monilia and oïdia.

Therefore, at the present time the exact relationship between monilia and sprue is not undisputed, and future and further work will be necessary in order to clear up this problem. We believe, however, that the finding of monilia-like organisms in the blood of a chronic case of sprue from Korea (which we[5] reported about a year ago), and the confirmation of this finding by Ashford in cases in Porto Rico, which fact he was so kind as to communicate to us, makes almost certain the necessity of relating some of the disturbances in sprue to this type of organism.

It is apparent that one cannot put these findings lightly aside; certainly it does not necessarily follow because an organism is present in the blood of a patient that such organism must bear a causal relationship to the disease. But it is equally certain that if an organism is very constantly found in the stool in a condition in which diarrhea is a cardinal symptom, and the same organism when administered by mouth will produce diarrhea in animals, and, finally, if the same organism can be found in the blood of the patient, as well as in the blood of the animal which was fed, then we must give most careful consideration to the role of that organism in that disease.

Probably the most telling arguments which have been raised against the relation of monilia or similar organisms to sprue have been the findings in cases of diarrhea and also in normal individuals. Thus, Ashford,[6] from Porto Rico, reported finding Monilia psilosis in 17 per cent of cases not sprue, but showing gastrointestinal disturbances, and 3 per cent of normal individuals. Dold,[7] in China, found monilia or related organism in 16 per cent of cases with diarrhea which were not sprue and similar organisms in 7.5 per cent of normal stools. Castellani also found monilia or oïdia in the stools of normal individuals, as well as in the stools of diarrheal cases, not sprue.

It is interesting to note that both Ashford and Dold found fungi more frequently in the stools of diarrheal cases which were not sprue than in the stools of normal individuals. It is, therefore, suggested that either the fungi are in some way related to the diarrheal conditions or that, as a result of abnormal conditions in the intestinal tract, the fungi are better able to gain a footing and persist there.

In connection then with these observations, we wish to report here upon a series of 32 cases which we have studied culturally, in 20 of which fungi have been isolated from the stool and, in some cases, from the blood.

The 20 cases in which fungi imperfecti were found can be divided into several groups: (1) A series of cases which were definitely diagnosed as tropical sprue, 7 having originated in Korea and 1 in Mexico; (2) a group of cases in which there was either a chronic diarrheal condition or an ill-defined gastrointestinal disturbance; (3) a group of cases in which there was an acute diarrheal condition but which, however, usually cleared up in a brief time.

The first case of sprue has already been referred to in our earlier publication, and we give here a brief abstract of the case as well as the findings.

Case I.—Dr. R. M. W., while in Korea, developed sprue. He returned to this country during the year 1922, and was put in touch with us through the kindness of Dr. J. E. Cook. When we saw him he complained of a sensation of distention, flatulency, indigestion and mild diarrhea; he slept poorly and was irritable. His general appearance was quite fair; he did not show emaciation. We obtained a specimen of stool and isolated a yeast-like organism. In addition, in a blood culture taken at the same time we obtained an organism identical with that found in the stool. In this case we find the organisms both in the blood and in the stool. The organism has not as yet been specifically identified, but it is either a monilia or a monilia-like organism.

Case II.—E. W., a patient of Dr. A. Taussig, had lived in Mexico for forty years. His health was good until June, 1922, when he had

a violent attack of vomiting with diarrhea; this lasted a week and was followed by complete recovery, except for some remaining weakness. In July diarrhea returned and continued intermittently until October. Then he began to have a sore mouth; gums, inner aspect of lips and especially the tongue were reddened, swollen and painful, so that he could hardly eat. This condition remained severe for three weeks, but did not entirely cease until the end of November. For several months the diarrhea was persistent; bowel movements massive, clay-colored, often foamy, usually extremely foul and occurring more frequently at night than during the day.

We isolated a monilia from the stool of this patient, but were unable to find a similar organism in the blood. The patient was treated with a vaccine, prepared from the organism, and showed improvement which, however, lasted only a few months. Eventually he left the city and died, according to the report we received, of anemia and asthenia.

The remaining 4 cases in this group (Cases III, IV, V and VI) were persons suffering from sprue acquired in Korea, and from them we obtained only specimens of stool. The disease was in a chronic form, and the patients had all been invalided to this country to recuperate. The specimens were sent to us through the kindness of Dr. E. M. Wilson. In 3 of these cases we isolated from the feces organisms similar to those found in the first case, and in the fourth we found an oöspora in the stool.

Thus, in all 6 cases of tropical sprue we were able to isolate fungi imperfecti from the feces, and in 1 of these cases the same organism was found in the blood.

In addition, we examined stools from 2 quiescent cases of sprue which had, like the last 4, originated in Korea, but we were unable to find monilia-like organisms in the specimens. They were both cases which did not show any symptoms at the time the specimens were taken, and the stools were certainly not sprue-like in character. However, in 75 per cent of the cases of sprue we found fungi imperfecti in the stools.

In the second group the first 2 cases, both chronic diarrheas, we are able to report through the kindness of Dr. J. W. Larimore. The abstracts of the histories are given here.

Case VII.—M. W. complained of diarrhea since January, 1922, which was worse and constant since June, 1922. Stools: Three movements daily, mostly in the morning after 5.30 A.M.; thin and watery and very foul; no foam, mucus or blood; "rush" movements follow large meals. Loss of weight from 160 to 120 pounds in eight months. Tongue very sore. Physical examination showed anemia malnutrition, dental caries, tongue red and fissured. Gastric anal-

ysis showed achlorhydria. A monilia was isolated from the stool, and a vaccine prepared from this organism. After administration of the vaccine the condition of the bowels was much improved to only slight frequency and to near normal form and consistency. The patient otherwise remained about stationary, with slight increase in hemoglobin.

CASE VIII.—M. S. complained of frequent stools and abdominal discomfort for five to six years. Stools: Two to four movements daily, often induced by eating, following in thirty minutes; thin, mushy, voluminous and foul. Some irritation of the anus. Weight: Stationary at 146 pounds. Examination showed nothing notable. Stool analysis: Dark brown, mushy, no gas, foam, mucus or blood. An oöspora was isolated from the stool and the vaccine prepared. Improvement of bowel condition was definite during and following vaccine treatment with restoration of normal character of stool, but movements continued twice daily and were increased with excitement.

CASE IX.—Mrs. L. W., a patient of Dr. M. Wachowiak, had diarrhea for eight months. It came on rather suddenly, six to eight or even ten stools a day, with no relief as a result of medical treatment; sugar diet aggravated condition. An oöspora, possibly similar to that called Oïdium asteroides by Castellani, was isolated from the stool and from the blood. The patient was treated with the vaccine prepared from the organism and the diarrhea cleared up entirely. Her condition has remained satisfactory for a period of a year.

CASE X.—F. R. R., a patient of Dr. W. Engelbach, began to have intestinal trouble in November, 1917, while the patient was in the army in France, with the appearance of mucus in the stool. This condition persisted until the spring of 1918, at which time there was an increase in the number of stools to eight to ten a day. Some loss of weight occurred, the exact amount not known, with the appearance of general weakness, and at about this time flatulency appeared. The condition persisted with exacerbations and remissions. The patient noticed that there was a definite aggravation following exercise. There was a fluctuation in the number of stools a day, varying from four and five to eight to ten. Monilia-like organisms were found in the stool but not in the blood of this case; a vaccine was prepared and, following the administration, there was marked improvement, although the frequency of bowel movements was not quite restored to normal. This improvement has lasted for about eight months, and the patient is better than at any time since the disease started.

Cases XI and XII have been reported in our earlier communication.

Case XI.—E. W., a patient of Dr. C. F. Wilhelmj, was located during the war at Camp MacArthur, where he came in contact with soldiers, who had previously served in the tropics, and some of whom were suffering with diarrhea. He did not have diarrhea while at Camp MacArthur, but after he was transferred he developed an attack of diarrhea of brief duration; however, intermittently thereafter this diarrheal condition lasted up to the time he was seen in the summer of 1922. His weight had fallen from 153 to 112 pounds. He did not show any stomatitis at any time; his stools were liquid and not sprue-like in character. Cultures of the feces and blood both showed the presence of a monilia-like organism.

Case XII.—B. R. was a patient at the Jewish Hospital of St. Louis, whom we were able to examine through the kindness of the physician of the medical service of that hospital. In 1921 he was operated upon for appendicitis. His convalescence was slow and he had considerable abdominal discomfort for many months afterward. Finally, in January, 1922, what was apparently an abscess in the abdominal wall was opened; the abscess cavity, from all appearances, communicated with a walled-off peritoneal abscess. This continued to discharge and failed to heal. While the patient suffered with intermittent and rather mild diarrhea, blood being present in the stool, at no time was the diarrhea of serious moment. Monilia-like organisms were found in the stool, in the discharge from the fistula and in the blood.

Case XIII.—C. F., a patient on the service of Dr. R. A. Kinsella at the Barnes Hospital, had a chronic infectious arthritis, envolving several joints, and also intermittent diarrhea. Frequently there was a discharge from the rectum, which was purulent. On proctoscopical examination a simple polyp was formed. In this case a monilia-like organism was found in the stool, but not in the blood. At the time we did not realize the possible significance of this finding and no vaccine was administered, this being at a rather early period in the course of our work.

Case XIV.—B. K. had been under observation of Dr. J. E. Cook for some years, with intermittent diarrhea of varying severity, showing from time to time blood and mucus in the stool, without, however, any very marked loss in weight or distinct discomfort. In this case we found a monilia-like organism in the stool, but no vaccine was used.

Case XV.—M. S., a patient of Dr. A. J. Kotkis, had had intermittent attacks of diarrhea for four years, with from two to six

bowel movements a day. Sometimes these attacks came on at night, but they were irregular in the time of appearance. At times the attacks were mild and of short duration, again they might be severe and persistent. No type of diet or medicinal treatment seemed to have controlled or modified the condition. A monilia was found in the stool and the patient was treated with a vaccine prepared from the organism, and only a slight beneficial effect was noted.

The third group represents a series of cases in which there was mostly an acute diarrhea, usually with spontaneous recovery, and in 1 case ending in death.

Case XVI.—F. T., a patient of Dr. Larimore, had a sudden "spell," after which he was unable to walk for eight weeks. Eight weeks before he was seen he developed a severe diarrhea after being constipated all his life; he had poor control of the rectum during these weeks. Loss of weight from 180 to 143 pounds in five months. The stool was semifluid and gassy. Gastric analysis showed achlorhydria. Here a monilia-like organism was isolated from the stool, but, as the patient died, no vaccine treatment was administered.

Case XVII.—C. B., a patient of Drs. Ehrenfest and Sale, was operated upon, December 22, 1922, for fibromyoma of the uterus, and a hysterectomy was performed. December 23 or 24 the patient began to have severe diarrheal attacks, the number of stools varying between eight and eighteen. This continued until December 30, and was associated with nausea and vomiting. The diarrhea subsided automatically without any particular specific treatment. A monilia-like organism was isolated from the stool of this case, which, as stated, recovered spontaneously, so that no vaccine treatment was called for.

Case XVIII.—M. B. was a patient of Drs. S. Simon and J. E. Cook. Seven days before admission to the hospital there had been a sudden onset of abdominal cramps, chills and fever of 103°, with ten to twelve loose stools, principally blood and mucus. This was associated with abdominal discomfort. Nothing in particular was evident on physical examination. No particular cause for diarrhea was evident during the stay in hospital. The number of stools became approximately normal after about eight to ten days. A true monilia was isolated from the stool in this case.

In 2 additional cases (XIX and XX) stools were sent to us. No history beyond the diagnosis of a chronic diarrhea of unknown origin was available. Both showed oöspora in the stools.

We then have here a series of 20 cases, including 6 of sprue in which there was a diarrhea, and in each one of them there was isolated from the stool a monilia, monilia-like organism or an oöspora. It should be mentioned that in all these cases amebic or bacillary dysentery and tuberculosis have been excluded in as far as was possible; that in all, therefore, the etiological factor was uncertain or unknown.

In 4 other cases, in which a diagnosis of either amebic dysentery or enteric tuberculosis was eventually made, we found no monilia in the stool; but in 1 of these a common yeast was found.

In 12 additional cases in which diarrhea was a prominent symptom, but in which no definite diagnosis concerning the causative factor could be made, we found no fungi imperfecti.

Thus, in 32 cases of diarrhea in which no specific diagnosis determining the cause of the gastrointestinal disturbance was made, or in which sprue was diagnosed, we found monilia or similar organisms in the feces in 62.5 per cent of the cases. If we omit the 8 cases of sprue and consider only the 24 cases of diarrhea of undetermined origin the fungi imperfecti were present in 58 per cent of the stools of this group.

Discussion. There naturally arises the question whether we are justified in assigning any etiological relation in these diarrheas to the fungi imperfecti.

In the first place: Is there any evidence that these organisms are associated with the production of gastrointestinal irritation leading to diarrhea? This can be answered in the affirmative, since in rabbits fed with certain of these organisms (monilia, monilia-like or oöspora) a diarrhea was produced with the appearance of the organism in the feces. The organisms were found in the blood of some of the animals, and at times at autopsy; lesions were also present in the liver and lungs from which we were able to isolate the organism. In a number of cases the fed rabbits died. We should state, however, that we have not as yet tested all of these organisms in animal experiments, but are at present carrying out such experiments.

Aside from this experimental evidence, it is generally recognized that yeasts act as cathartics; however, if the common yeasts are fed to animals they rapidly disappear from the stool; on the other hand, if these fungi imperfecti are fed to rabbits they persist in the stool for considerable periods. Their effect then is apparently more than merely a transitory one due to the introduction by feeding. Anderson[8] has shown that common yeasts fed to man also rapidly disappeared from the stool, but Monilia psilosis persisted in the stool for a long time. There is, therefore, apparently a difference between the relationship of wild yeasts to the mammalian organism and the relationship of at least some of these fungi imperfecti to the same organism.

There still remains the question which will naturally arise in every mind: To what extent do we find organism similar to these mentioned above in the stools of normal individuals? As we have stated above, Ashford, Castellani and Dold have all found similar organisms in the stools of normal individuals. Anderson some years ago investigated the fungi occurring in the stools of normal individuals and found yeasts or yeast-like organisms in 47 per cent of the ninety-eight normal stools examined. In individuals with diarrhea he found similar organisms in 46 per cent out of thirty-seven examined. However, it is not clear from his reports how many of the organisms found were of the monilia or oöspora type; apparently most of them were of the common yeast type, and only about 4 seem to have been either monilia or oöspora. His results are, therefore, not directly available toward clarifying this point.

We have examined the stools of a number of normal individuals, and found in a first series common yeasts or fungi imperfecti in 38.5 per cent of sixty-six stools. The majority of these, however, are neither monilia or oöspora; in only 2 cases were monilia-like organisms isolated, and in 1 additional case an oöspora was found. We have recently examined a second series of twenty-four normal stools, and here 1 monilia and 5 oöspora, resembling these found in the diarrheal stools, were found. Thus, in ninety stools from normal individuals we find these fungi imperfecti in only 10 per cent of the stools. From the evidence of the investigations of others as well as our own work, it seems that organisms of this type are occasionally found in the stool of normal individuals, but by no means as frequently as in the stools of individuals with diarrhea.

Furthermore, we believe that the finding of fungi imperfecti in the blood in certain of these cases adds very materially to the weight of the evidence. It is true that they were not found in the blood in all cases; but, of course, in many other diseases, where we know a bacteremia exists, we do not constantly find organisms in the blood cultures. It is possible that our technic is as yet imperfect, and that with improvement in this respect our findings of these organisms in the blood may become more frequent.

Nevertheless we have found fungi imperfecti in the blood stream in 4 of our 20 positive cases—1 of sprue and 3 of chronic diarrhea. In 3 cases there were monilia-like organisms and in the fourth an oöspora. It seems hardly plausible that an organism, present in the intestinal canal, capable of causing gastrointestinal disturbance and also present in the blood stream, should not have some relationship to the patient's condition.

Summary. If then we summarize the evidence brought together here it runs somewhat as follows:

1. In a series of cases in which diarrhea was a prominent, if not the most prominent symptom, we have been able to demonstrate in the stools the presence of fungi, monilia or similar organisms in

62.5 per cent of these cases. In some of these cases identical organisms have been demonstrated in the blood stream.

2. A number of these organisms have been fed to rabbits, and in such animals they have produced diarrhea—in some cases even death. In some of these animals the organisms have been recovered from the blood and from lesions in the internal organs.

3. Monilia or similar organisms are to be found in the stools of normal individuals in a small percentage of cases, in a much smaller percentage than where a diarrhea exists. Relatively in normal individuals the occurrence of these fungi in the feces is infrequent.

4. Are we then justified in considering these organisms as having any bearing upon the diarrheas in these cases? We are at present inclined to believe that in those specific conditions, as in sprue—in which fungi imperfecti are generally found (we found them in 75 per cent of our cases)—some causal relation exists between the organism and the symptoms. We believe that our finding, namely that the organism may be present in the blood stream, very materially strengthens this viewpoint. We believe that it will be difficult to deny a relationship between the symptoms of a patient and an organism found in both stool and blood of a case of diarrhea not diagnosed as sprue.

5. While we realize the possible fallacy in attempting to base any conclusions regarding etiology upon the results of vaccine therapy, nevertheless the improvement showed in certain of these cases following vaccine therapy, suggests a possible relationship existing between these fungi and the disease. Our results do not warrant us in going any further than this, but we suspect that in many cases, where there exists a chronic diarrhea which cannot be explained on any other basis, organisms of this type may be factors. We wish to make clear that, of course, we do not think nor wish to suggest that fungi play a part in all diarrheas, even though no causal agent may be evident.

6. Finally, we present this series of cases, our results and our tentative conclusions simply as a suggestion for further investigation in this field.

NOTE.—A further study, since this article went to press, of the so-called monilia-like organisms has demonstrated that they should be classed as monilia.

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TWO CASES OF MYCOTIC ANEURYSM, GONOCOCCAL AND PNEUMOCOCCAL IN ORIGIN.

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Mycotic aneurysms occur not infrequently during the course of an acute endocarditis or other acute infectious diseases. They form a distinct group, and, since relatively few are recognized during life, are of interest chiefly from the viewpoint of pathology.

The first description of an embolomycotic aneurysm apparently was made by Koch in 1851. His case was that of a ruptured mycotic aneurysm of the superior mesenteric artery which developed during an acute endocarditis. Since then the work of Ponfick, Eppinger and other investigators have placed this type of aneurysm on a definite etiological and pathological basis.

This type of aneurysm occurs for the most part in young adults, in marked contrast to the age period in which the luetic and arteriosclerotic aneurysms are found. It usually develops in connection with a concomitant acute endocarditis; occasionally, however, no primary endocarditis is present in the heart. The visceral and peripheral arteries in particular are sites of embolomycotic aneurysms; various portions of the aorta, however, may be involved by this definite pathological process. Many different bacteria such as streptococcus, staphylococcus, pneumococcus, the typhoid bacillus and even the gonococcus have given rise to this peculiar type of aneurysm.

The mechanism of formation of an aneurysm occurring in the smaller arteries is quite simple. This is due to an infected embolus plugging the artery usually at a point of bifurcation. The bacteria which gain entrance to the wall of the artery produce a mesaortitis with a resultant destruction of the elastic and muscular elements of the wall. Eventually the remaining parts of the media and adventitia bulge outward to form the sac of the aneurysm. However, not all cases observed, especially those developing in the aorta, follow this definite pathological sequence. Aneurysms occurring in the aorta are assumed to be due either to direct injury to the intima by bacteria or to the lodgment of an infected or bacterial embolus within the media. It is conceivable, that a congenital anomaly or an arteriosclerotic lesion may serve as a point of lessened resistance, and thus favor the direct lodgment of bacteria with resultant necrosis and aneurysm formation.

Many of the cases of mycotic aneurysms are associated with a latent symptomatology, so that their detection is not possible during life. Others, especially those occurring in the peripheral

arteries, give evidence of their presence by pain and swelling at the site of aneurysm. Occasionally the first indications of a mycotic aneurysm are the symptoms of internal hemorrhage due to rupture.

The 2 cases which comprise the subject of this article are of particular interest on account of the etiology and location of the aneurysms.

CASE I.—A female, housewife, aged twenty-nine years, with a history of a vaginal discharge of one and a half year's duration following a miscarriage, suffered for a period of two months prior to admission from dysuria, urgency, fever, chills, sweating, dyspnea and pain beneath the sternum. She had become progressively weaker and developed a tender spot on one toe.

Physical examination revealed emaciation, pallor, slight clubbing of fingers and subcutaneous petechiæ. The heart was slightly enlarged to the left and systolic thrills were present at the apex and at the pulmonic area. Systolic and diastolic murmurs were heard at the apex, and over the base a to-and-fro murmur was obtained. The blood-pressure was 128/54. The spleen was definitely palpable. The cervix was slightly reddened and contained a moderate amount of purulent discharge.

There was a moderate secondary anemia with a leukocytosis which ran as high as 31,950 at one examination. The urine showed albumin, red and white cells and casts at certain times. Four blood cultures were negative. The Wassermann reaction was negative. The gonococcus complement-fixation test was positive.

During the patient's seventy-one days in the hospital she ran a typical course of sepsis with various embolic phenomena. She developed a severe secondary anemia and became considerable emaciated before death.

Abstract of Necropsy. Anatomical Diagnosis: Mycotic aneurysms of ascending aorta (gonococcus); acute aortic endocarditis (gonococcus); organizing fibrinous pericarditis (gonococcus); hypertrophy and dilatation of the heart; bronchopneumonia; infarcts of spleen; ascites; chronic pleuritis.

General examination of the body showed petechiæ and several decubiti. The peritoneal cavity contained 1400 cc of serous fluid. Fibrous adhesions were present between the spleen and diaphragm. The pleural cavities contained old fibrous adhesions.

The peritoneal cavity contained 200 cc of a serofibrinous fluid. The pericardium was covered with a thick exudate of yellowish fibrin which was thrown up into ridges producing a shaggy appearance. In several places the exudate was reddish in color, tough and adherent, due to organization.

The heart was enlarged, weighing about 450 gm. The aortic valve was slightly thickened and contained soft, granular, pinkish vegetations 3 to 4 mm. in diameter. The arch of the aorta was dilated. Immediately above the aortic valve were several small

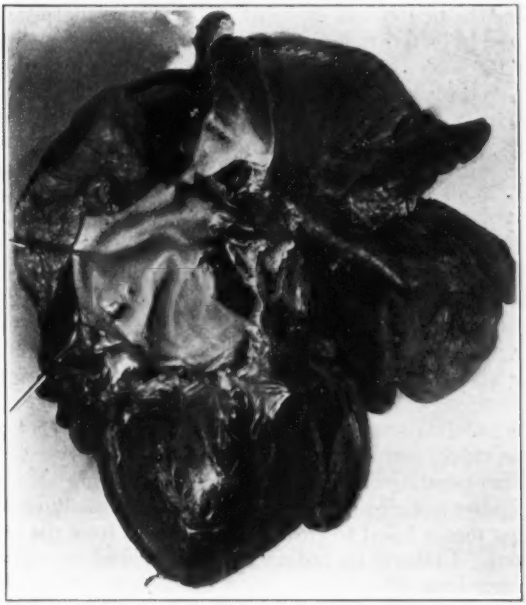

FIG. 1.—Case I. Mycotic aneurysm (gonococcus). Note also the fibrinous exudate on the pericardium.

FIG. 2.—Case I. Mycotic aneurysm (gonococcus). High power of vegetations showing clumps of biscuit-shaped organisms.

aneurysms 0.5 to 1 cm. in diameter. They were sharply outlined, bulged out from the right side of the aorta and were filled with granular thrombi. On the posterior aspect of the ascending aorta near the arch was another large aneurysm extending inferiorly and to the right beneath the bifurcation of the trachea for a distance of 4.5 cm. It measured 2.5 cm. in diameter, was sharply outlined and filled with granular thrombi. At one point on the orifice of this sac, a small dissecting aneurysm took origin and extended along the ascending aorta for a distance of 1.5 cm. The remainder of the heart and aorta was negative.

The lungs showed patches of bronchopneumonia. There was no communication between the large aneurysm and the right lung. The spleen was slightly enlarged and contained several small infarcts. The kidneys were somewhat pale and not unusual on section. The uterus and adnexa showed no signs of any inflammatory process.

Smears from the exudate on the pericardium, the vegetations on the aortic valve, and from the thombi in the aneurysms revealed many Gram-negative diplococci in colony formation. Many of the Gram-negative biscuit-shaped organisms were intracellular. Special starch agar media failed to grow the gonococcus from the blood and vegetations. Cultures on ordinary media showed several contaminating organisms.

Microscopical sections of the vegetations stained with Giemsa disclosed many colonies of bacteria and scattered isolated bacteria occurring as flattened diplococci. Many bacteria were incorporated in polymorphonuclear leukocytes. Sections of the spleen showed infarction. Kidney sections revealed small thrombi in the glomeruli with partial hyalinization. Sections of the uterus were negative.

Case II.—A school boy, aged ten and a half years, suffered from increasing cough and fever. At approximately the age of two, the patient had developed a mild endocarditis, which in subsequent years did not incapacitate him. The present illness began four weeks before death with an attack of a then prevailing epidemic of nasopharyngitis. At no time was he very ill, and the chief symptoms were cough and fever. Increasing frequency of cough resulted in a consultation at which nothing abnormal could be found in the chest. A few days before death the patient had respiratory distress. While in apparently good condition, he had a sudden hemorrhage from the mouth and died immediately.

Abstract of Autopsy. The autopsy was performed in a private home after the body had been embalmed.

Anatomical Diagnosis: Mycotic aneurysm (pneumococcus) of descending aorta with rupture into esophagus and lung; slight mitral endocarditis (chronic); congenital anomaly of thoracic aorta; slight hypertrophy of the heart; acute splenitis.

In the left pleural cavity, the medial surfaces of both lobes of the

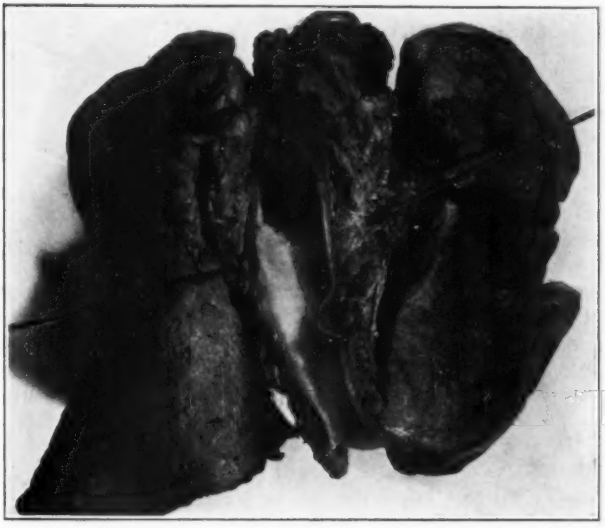

FIG. 3.—Case II. Mycotic aneurysm (pneumococcus). Aneurysm filled with thrombus in descending aorta.

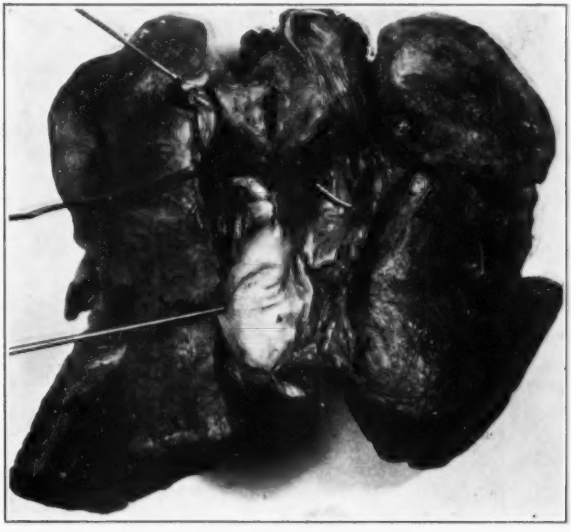

FIG. 4.—Case II. Mycotic aneurysm (pneumococcus). Aorta pulled over to the right so as to show the rupture into the esophagus.

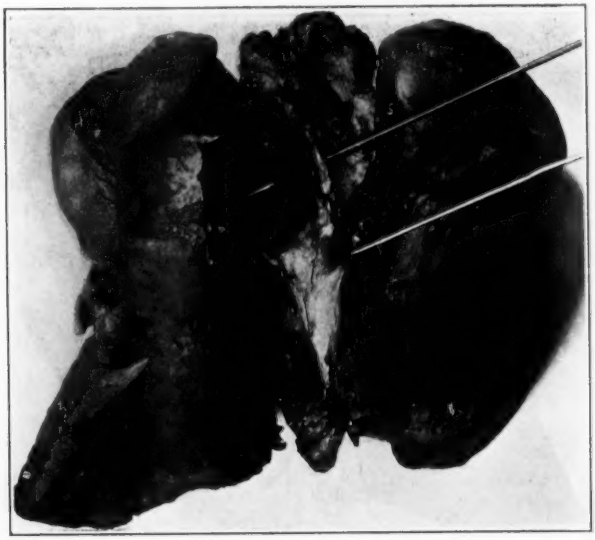

FIG. 5.—Case II. Mycotic aneurysm (pneumococcus). Aorta and esophagus drawn over to the right so as to reveal the dissection in prevertebral space and adhesions to left lung.

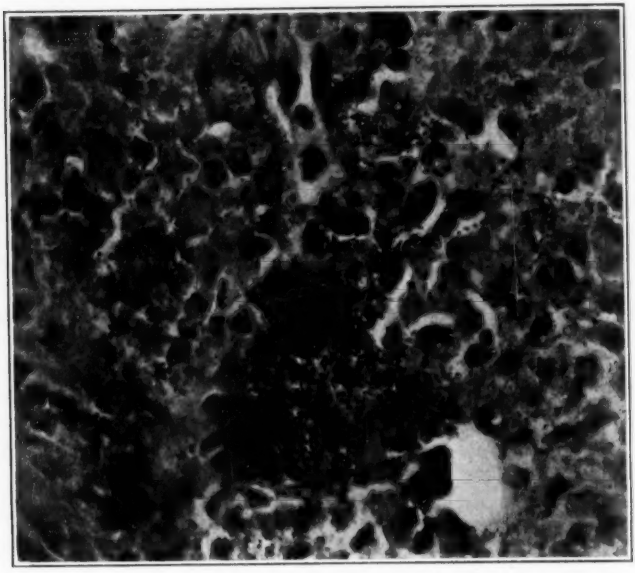

FIG. 6.—Case II. Mycotic aneurysm (pneumococcus). High power of wall of aorta showing lanceolate diplococci and inflammatory reaction.

lung were tightly adherent to a swelling over the vertebræ. Separation of the adhesions revealed a cavity 5 cm. in diameter, filled with a peculiar friable clot. The adjacent lung tissue was somewhat firm.

The heart was hypertrophied. There was a rather pronounced thickening of the junction of the anterior and posterior segments on the right side of the mitral valve. The ascending aorta, up to the origin of the innominate artery, was slightly dilated, measuring 4 cm. in circumference. A marked constriction of the aorta formed by a yellowish ridge, was found 2.5 cm. below the origin of the left subclavian artery. Above the constriction, there was slight thinning and bulging of the aortic wall with some barely visible transverse striations. Below the constriction was a marked dilation with a hole involving the anterior and left wall of the aorta. The irregularly outlined orifice extended downward for 3.5 cm. and involved at least five-sixths of the circumference of the aorta. At one point a sharp break in the wall of the aorta opened into a cavity filled with gray crumbly clot. This cavity was walled off by vertebræ and lung tissue. The esophagus was markedly deviated to the right and contained a cavity on the left side measuring 5.5 cm. vertically and 3 cm. laterally. This cavity communicated with the aortic blood stream by means of numerous ragged openings through the aneurysmal wall. The left primary bronchus was pressed downward and forward, but showed no absorption of cartilage.

The lungs showed small red areas due to insufflation of blood. The spleen was enlarged, soft, almost diffluent. The remaining organs were negative.

Sections through the aortic wall at the orifice of the aneurysm disclosed marked necrosis extending from the edge into the wall of the aorta. For a considerable distance the aorta could be recognized only by the remaining elastic laminæ, while the smooth muscle was replaced by necrotic tissue and the polymorphonuclear leukocytes. Giemsa stained sections showed many diplococci both intracellular and extracellular, which could not be demonstrated by Gram's stain. The striking thing in the aortic wall at the edge of the aneurysm was the definite abscess formation in addition to the diffuse infiltration of polymorphonuclear leukocytes.

Discussion. The first case is evidently one on gonococcus septicemia. The history of vaginal discharge previous to the onset of illness, the absence of a history of rheumatism, the presence of signs of valvular disease most marked over the aortic valve, the inability to obtain a positive blood culture and the positive gonococcus complement-fixation test established this diagnosis during life. The identification of an organism possessing the tinctorial and morphological characteristics of the gonococcus at autopsy further substantiated the diagnosis of gonococcus septicemia even though there were no localizing lesions found in the genital tract.

Thayer,[3] in a recent review of gonorrheal endocarditis found that the gonococcus usually involves healthy, previous unaffected valves; that the aortic valve is most commonly involved; that grave constitutional symptoms are present; and that gonorrheal endocarditis is a malignant process, pursuing a progressive and fatal course usually within five to nine weeks. The writer's case, though of longer duration, fifteen to eighteen weeks, possessed all the other characteristics of gonorrheal endocarditis. In this case the pericarditis, also due to the gonococcus, arose by direct extension of the infection through the wall of the largest aneurysm into the pericardial sac.

The second case illustrates what an extensive process there may be in the aorta with relatively few or no symptoms, except those due to pressure. The process was acute, extending over a period of only four weeks. The mycotic aneurysm developed without any associated acute endocarditis and no doubt was due to direct injury of the intima by the pneumococcus, at the site of the slight, presumably congenital, constriction noted below the arch.

Conclusions. 1. The etiological factor has been determined with fair accuracy in two cases of mycotic aneurysms.

2. One case due to the gonococcus was insidious in onset, protracted in duration and presented all the classical signs and symptoms of a septicemia; the other due to the pneumococcus was of an acute nature and gave but relatively few localizing signs.

3. The possibility of the formation and rupture of mycotic aneurysms should be borne in mind in all cases of acute infectious diseases.

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2. Lewis and Schrager: Jour. Am. Med. Assn., 1909, **53**, 1808.
3. Thayer, W. S.: Johns Hopkins Hosp. Bull., 1922, **33**, 361.

THE HUMAN DYING HEART.

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Introduction. In the physical processes of individual organs, death is a more or less relative phenomenon. This applies with especial emphasis to the heart.

There are various stages in its progressive functional and structural deterioration. In the early stages, as the probable result of nervous influences, there may be a cessation of function which under stimulation can return to normal. What may appear clinically as absolute death may in reality be only a depression of outward manifestations. Second, because of chemical changes in the blood or in the tissues, the capacity to function may be so far depressed that its recovery under stimulation is unlikely. The final stage, from which no recovery is possible, is the dissolution or absolute death of the tissue both in chemical reaction and in microscopical appearance. It is during these stages that the fascinating borderline phenomena between life and death take place.

The controlling factors of the heart's action may be divided into:

1. The central regulating and controlling mechanism in the medulla.

2. The autonomic function situated in the heart as specialized nodal tissue.

3. The heart muscle itself and its blood supply.

It is probable that all these factors are terminally attacked in varying proportions, the degree depending upon their vulnerability.

It may be assumed theoretically that in the derangement of the nervous control of the cardiac mechanism the first disturbances would affect the main controlling centers. With depression of these the subsidiary centers would then become dominant.

One of the important changes that takes place in the dying individual is inadequate tissue oxidation with an accumulation of carbon dioxide. The premonitory manifestations in the dying heart are partly the result of this chemical change. The vagus centers in the medulla are stimulated, producing inhibition of the most susceptible heart regions; that is, the atrial node and the conducting tissue in the heart are depressed. Because of the oxygen deficiency, the muscle tissue may also evince peculiarities of action.

The Mechanism of the Dying Heart. The phenomena of death as they are revealed by the electrocardiogram relate to the disturbances of function immediately preceding the absolute cessation of all heart activity.

It was formerly a point of considerable interest as to what portion of the heart is the *ultimum moriens*. It was found in a number of studies of animals during asphyxia that the most viable parts of the heart are located in the right auricle.[1] At times, in the dying heart, the auricular appendage showed the strongest hold on life and was the last part to retain the power of contraction. Others had found that the region about the mouth of the vena cava manifested contractions after all other regions of the heart became quiescent,[2] and

[1] Eyster and Meek: Heart, 1913–1914, **5**, 137.
[2] MacWilliams: Jour. Physiol., 1888, **9**, 167.

still others found it at various regions between the atrial node and the auriculoventricular node.[3]

It may be that in the dying asphyxiated heart the impulse arises in a region different from that in which it arose in the same heart beating under normal conditions. It must be remembered also that the properties of the heart muscle are present in varying degrees relative to each other in different parts of the heart.[4] Thus certain regions may show no visible contractions, although automaticity or excitation may arise from them. That is, cessation of all functions does not take place at the same time.

It has been shown that after complete auriculoventricular dissociation from asphyxia (in the cat) the auricular contractions almost always abruptly disappear.[5] This is due to the abrupt termination of the function of the sino-auricular node, the auriculoventricular node continuing to control the ventricle. When this happens the heart will not recover although re-oxygenated. This change would account fully for the end curves in simple asphyxia and in certain of the curves of the dying human heart.

The beats of the dying heart are slowly conducted, and the contraction waves may often be seen to originate near the mouths of the great veins and to be conducted from them.[6]

In a very extensive experimental study on dogs and rabbits by Yamada, death of the heart was induced by a great variety of mechanical causes, by the action of chemicals, by drugs and by anaphylaxis.[7] In these experiments the general sequence of events corresponded to those found in asphyxia.

There was first a slowing of the heart action with early failure of the atrial node which was often temporary and caused by vagus stimulation. This was followed by dissociation between the auricles and ventricles. The auricular contractions stopped more abruptly than the ventricular. The nodal control of the ventricles lasted a varying length of time, during which period the rate of the auricles and ventricles slowed. There was usually a recovery of sinus control of the heart, again followed by complete dissociation. Either the auricles or the ventricles persisted longer. In the preterminal stage, there were variations in the form of the auricular and ventricular waves with characteristic and striking changes. There also occurred attacks of auricular or ventricular tachysystole. Some of these have their analogue in the dying human heart.

That the main changes were due to vagus control was shown in a parallel series of experiments after vagus section. In these sinus arrhythmia disappeared before asphyxiation and the tachycardia

[3] Hirschfelder and Eyster: Am. Jour. Physiol., 1907, **18**, 221.
[4] Hoffmann: Arch. f. d. ges. Physiol., 1910, **133**, 552.
[5] Lewis, White and Meakins: Heart, 1913–1914, **5**, 289.
[6] Lewis: Mechanism and Graphic Registration of the Heart-beat, 1921, Chap. V, p. 70.
[7] Yamada: Mitt. a. d. med. Fakult., Univ. Tokyo, 1920, **25**, 97.

persisted for a long time. The early bradycardia and complete or incomplete heart-block in unvagotomized animals were thus shown to be due to central vagus stimulation. The abrupt cessation of the auricular contractions, more sudden than the ventricular, is explained by the greater sensitiveness of the atrial node than the auriculoventricular node to vagus stimulation. The periods of ventricular tachysystole that occurred were explained by cessation of the inhibitory action of the vagi and possibly also by stimulation of the accelerators. The impulse formation first migrated to the auriculoventricular node and then to some tertiary ventricular center. The latter produced abnormal ventricular complexes. The auricular contractions continued for a period after the ventricles had ceased beating.

Some of the vagus effects may be due to peripheral irritation of its endings in the lungs, reflexly causing complete heart-block. The occurrence of ventricular extrasystoles may be the result of extracardial vagus effects. In cases of embolism in the coronary artery, they may be due to the direct presence of air in the heart, reflexly affecting the vagi.

It seems probable that these changes in the rate and in the form of the complexes are dependent on changes in vagus tone. Diminution of the size of *P* and *T* waves occurring with periods of slow rate resemble the electrical complexes seen when the vagus tone is raised.[8]

It has been shown that part of any of the cardiac centers will induce the same rhythm as the entire center.[9] This is especially true for the veins and sinus and less for the auriculoventricular node and the bulbus. This also supports the view that vagus influences induce the early changes in the mechanism of the dying heart. Since the vagus would influence the nodal regions in its entirety more likely than would a change in the circulatory supply, the abrupt cessation of sinus rhythm also suggests a vagus effect.

The termination of attacks of ventricular fibrillation in death has been repeatedly observed.[10] The heart rarely recovers its normal mechanism.[11]

The Human Dying Heart. The first electrocardiographic study of the human dying heart was presented very briefly before a medical society in Germany in 1911.[12] In three fatal cases of diphtheria, there were found variable and abnormal *QRS* complexes. In 1 case, at least, there was complete auriculoventricular dissociation.

Seven patients dying from acute infectious diseases without cardiac involvement were studied by means of the electrocardiograph

[8] Rothberger and Winterberg: Arch. f. d. ges. Physiol., 1910, **135**, 506.
[9] v. Skramlik: Arch. f. Physiol., 1920, **183**, 109.
[10] Levy: Brit. Med. Jour., 1914, **2**, 502.
[11] Robinson and Bredeck: Arch. Int. Med., 1917, **20**, 725.
[12] Rohmer: München. med. Wchnschr., 1911, **58**, 2358.

in 1912.[13] In 4 of these, the ventricle outlasted the auricle and in 2 the opposite occurred. In 1 case, both stopped at apparently the same time. Arrhythmias occurred with delay in conduction time in 5 cases and other arrhythmias such as heart-block, ventricular extrasystoles, tachycardia and ventricular fibrillation took place without characteristic sequence.

"Characteristic changes in the ventricular complex of the electrocardiograms occurred in all the records. They consisted of a decrease in the size of the *R* wave and an increase in the size of the *T* wave, and a tendency to a fusion of these waves. There was usually but little change in the duration of the ventricular complexes as the cardiac activity gradually ceased. The change in the form of the ventricular electrical complexes indicates that the course of the stimulus and the manner of the contraction of the muscle were abnormal. The fact that the *R* wave became gradually prolonged suggests that the conduction of the stimulus through the ventricular walls became delayed as the heart died. The fact that after death there is a continuation of cardiac muscular activity sufficient to cause a difference in electrical potential between the two sides of the body does not necessarily mean that a ventricular systole in the sense of muscular shortening takes place. It has been observed experimentally that well defined electrical complexes may be caused by cardiac activity which cannot be seen or recorded graphically. As the duration of the ventricular complexes characteristic of the dying heart usually does not differ markedly from the duration of the complexes before clinical death, it seems probable that the entire musculature of the ventricles participates in the contraction; as definite shortening, or at least a marked change in duration, would be expected if only a part of the ventricular musculature participated in the activity which produced the complex."

Three other cases with terminal records of dying hearts were reported.[14] All were cases of cardiac failure with myocarditis. In these, clinically, there was marked impairment of the respiratory function with rapidly increasing insufficiency of oxygen and accumulation of carbon dioxide. There was slowing of the heart-rate with manifest auriculoventricular nodal control. There were periods of auricular and ventricular fibrillation and paroxysmal tachycardia of various types. There was usually a decrease in the amplitude of the main waves and widening of the *QRS* wave; the *T* wave became negative in 1 of the cases.

In an experimental study on the effects of low oxygen tension on the heart mechanism it was found that until a certain critical stage in the anoxemia is reached, the general changes in the electrocardiogram are slight.[15] These consist of shortened *P–R* interval

[13] Robinson: Jour. Exper. Med., 1912, **16**, 291.
[14] Dieuaide and Davidson: Arch. Int. Med., 1921, **28**, 663.
[15] Greene: Arch. Int. Med., 1921, **27**, 517; Am. Jour. Physiol., 1922, **60**, 155.

(increased conduction rate), coincident with increased heart-rate, decrease in total time of the R–T interval, decreased amplitude of the T wave with maximum retardation toward the terminal phase, and sometimes a diphasic or negative T wave.

With extreme oxygen want, there occur great slowing of rate; progressive descending displacement of the pacemaker, or center of rhythm production, toward and into the auriculoventricular node; and interference with normal conduction leading to dissociation. Later, conduction is suppressed with maintenance of auricular beats. There is also suppression of cardiac function in the descending direction, both as to rhythm production and conduction.

The changes that take place in the auricular complex may be very varied and, for the convenience of description, may be said to present the following types: Normal, inverted, diphasic, sudden rise with gradual fall, notched, double, auricular flutter and auricular fibrillation.

These may be combined with deformities of the ventricular excitation wave, which also for the convenience of description may be designated as follows: Normal, notching and widening of R, lower amplitude of R, union of R and T, inversion of T, absence of T, diphasic ventricular wave, ventricular flutter, ventricular fibrillation and abortive ventricular fibrillation.

We purpose in this communication to report the study of the dying human heart in 7 cases. In these, records were obtained for some time previous to and during the various stages of death. In all we obtained all or some of the last electrical complexes which followed the period of clinical death.

History Report. CASE I.—L. S., aged thirty-six years, was observed as a case of lobar pneumonia.

Important in the history of this patient was the persistent nasal obstruction for two years. During this time he suffered from frontal headaches of increasing frequency and severity. For three months before he died they were continuous. There was no precordial pain, dyspnea or palpitation.

Physical examination revealed almost complete nasal obstruction to breathing and total deafness of the right ear and less of the left ear. The heart was enlarged; its sounds were fair. The blood pressure was 100/60 mm.

The urine was negative. The blood Wassermann test was negative and the blood chemistry was negative. The blood showed about 6000 leukocytes, 60 per cent polymorphonuclears and 40 per cent large mononuclears. Roentgen-ray showed clouding of the antra. The temperature was normal.

Course: Following a nasal operation for turbinate-septal adhesions, the temperature rose to 104° F. and remained high to the end. The patient's condition became poor the day before he died. There

was cyanosis and bronchial breathing over the lower pulmonary lobes posteriorly. He died with cardiac failure.

Diagnosis: Bilateral lobar pneumonia.

Electrocardiographic Studies. Some hours before the patient died, the heart showed tachycardia, a rate of 125 per minute, slight left ventricular preponderance and P wave finely notched in leads I and II. (Fig. 1*a*).

The terminal records were taken in Lead II. Respiration stopped about two minutes before the audible heart beats. Shortly before clinical death there was distinct evidence of sinus arrhythmia. This was not as marked throughout the record but occurred rather spasmodically.

A few minutes before death, however, there was slowing of the sinus rate with marked sinus arrhythmia. At one point about seven minutes before the end of the record, the auricular contraction seemed to occur doubled (*b*). A minute later there was no evidence of sinus function and the P wave was suddenly lost from the electrocardiogram. The ventricular wave showed no change (*c*). The failure of the sinus to act was promptly replaced by nodal rhythm after a delay of 0.07 second.

The nodal rate increased slightly and progressively. At the same time, the QRS wave widened gradually and became slightly notched (*d*). In occasional cycles its course through the ventricles was aberrant. The origin of some of these beats was in the region of the auriculoventricular node, showing an irritability of the junctional tissue. Preceding two of these nodal cycles, a diphasic P wave occurred, with shortening of the P–R interval. (These are not reproduced in the figure.) Soon after this, there was a resumption of sinus rhythm with no delay in conduction. The P wave, however, was somewhat changed in contour; it was small with an abrupt elevation and a gradual fall (*d*).

The sinus rate continued slightly faster than the preceding nodal rate, without arrhythmia. The QRS complex had meanwhile become considerably widened with very much notching and thickening of the ascending limb (*e*).

Conduction, during all this time, was rather quick, the P–R interval being about 0.08 second. Suddenly, the sinus failed and the auricular beats were again lost. The nodal beats were slower except for irregular paroxysms, as in the first part of strip *f*. When the sinus did recover, it found a partial block, the P–R interval being prolonged to 0.48 second (*g*).

The auricular and ventricular rates were about the same, 67 beats a minute. The auricle, however, progressively slowed with slight variation in conduction defect and at times failure of the sinus.

The main deflections of the QRS wave diminished in amplitude or voltage and became more and more continuous with T. The

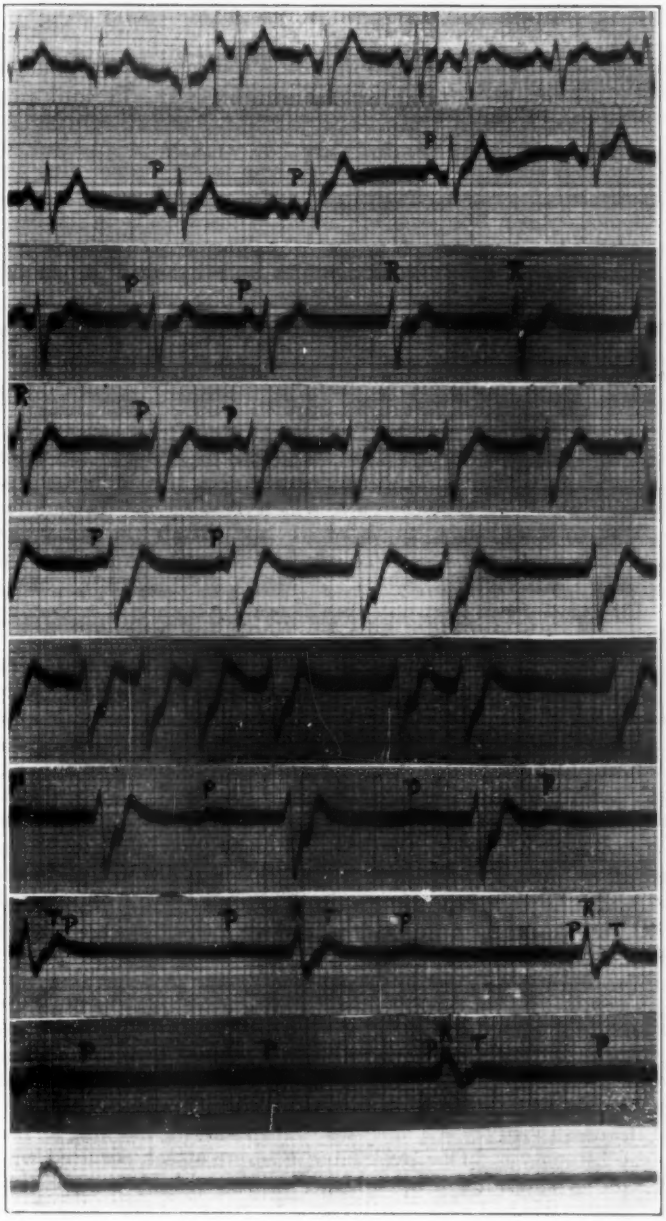

FIG. 1.*—Sequence of prints of the dying heart in Case I, analyzed in the text.

* In all photographs, (except Fig. 4): Abscissæ 1 division = 0.04 second. Ordinates 1 division = 10^{-4} volts. The strips are designated alphabetically from above down.

sinus rate continued at 67 and the ventricular rate at 25 per minute with complete auriculoventricular dissociation (*h-i*).

The intervals between the last few ventricular cycles were 5 to 7 seconds. Sinus activity was evidenced by *P* waves at a rate of about 65 per minute for a period of about thirty seconds after the last cycle (*j*).

Summary and Discussion of Case I. Thus we have in this case, the following sequence of events: (1) Sinus arrhythmia, depression and failure; (2) nodal rhythm with its irritability; (3) bundle-branch conduction failure or intraventricular conduction defect; (4) intermittent recovery and exhaustion of the sinus; (5) progressive nodal exhaustion with changes in the *QRS* and *T* waves; (6) terminal sinus rhythmic impulses for a long period after the last nodal cycle.

It is with some doubt that the wave in strip "*b*" is spoken of as a double auricular wave. There are several reasons why this interpretation can be given. Although not exactly a reproduction, its contour resembles the other waves in several ways. Its duration is the same, its height, angles of rise and fall are the same, and especially pertinent is its notching which very much resembles the other *P* waves.

It is very interesting to note that it occurs at the end of expiration. Inspiration is apparently indicated in the very fine fibrillatory waves during the next cycle. This may have been the patient's last gasp for breath, and with this there is a general elevation of the entire isoelectric level. What is difficult to explain is the occurrence of normal conduction during the refractory period following the abnormal wave. But, when the vagi are stimulated, the absolute refractory period of the muscle is greatly reduced.[16] It is also hard to see why the ventricular cycle did not immediately follow the first *P* wave. One must postulate a momentary blocking of the premature stimulus. It is thus a matter of conjecture as to the exact interpretation, yet we are loathe to dismiss it as an artefact.

The remainder of the record is almost self-explanatory and requires no further discussion.

Case II.—S. K., aged forty-nine years, was observed as a case of cardiorenal disease.

About four months before death, after a heavy meal, the patient slept a short time and suddenly awoke unable to breathe. During that night he had several such attacks with a fearful sensation as if the chest were pressed in a vice. The following morning he had some hemoptysis. One week later, a severe attack occurred with a sense of impending death which was relieved by heat applied to his chest. He had many similar attacks, the worst occurring about three weeks before death.

[16] Lewis, Drury and Iliescu: Heart, 1921, **8**, 311.

Physical examination showed slight cyanosis and dyspnea. There were a few rales posteriorly at the bases of both lungs. The heart was enlarged both to the left and right. Over the entire precordium, but heard loudest at the aortic area, there was a systolic and diastolic murmur. Over the mitral area the systolic murmur was rough, but not transmitted. Corrigan and capillary pulses and a pistol-shot sound in the brachials were present. The liver and spleen were just palpable below the costal margin. There was slight edema of the extremities and clubbing of the fingers.

The urine showed a moderate amount of albumin and hyalin and granular casts. The phenolsulphonephthalein test showed 20 per cent in two hours. The blood count showed 12,400 leukocytes and 70 per cent polymorphonuclears. The blood Wassermann test was weakly positive, but the spinal fluid was negative. Roentgen-ray examination showed marked enlargement of the heart to the right and left. There was also pneumonic infiltration and some fluid on the right side. The temperature was about 100° F. throughout. Blood cultures were negative. The blood-pressure was about 150/66 mm. The pulse-rate was about 100. Respirations were about 30 per minute at first and about 40 toward the end.

Course: Three days before death, the patient became more stuporous and irrational with marked respiratory distress.

Diagnosis: Chronic cardiovalvular disease and chronic parenchymatous nephritis.

Autopsy findings showed chronic congestion of the lungs. The heart was very much hypertrophied and the left ventricle was greatly dilated. The muscle was firm and smooth. The edges of the aortic valves were very thick and the seat of numerous large white nodular firm vegetations. The bases of the valves were thin and free from thickening. The mitral valve was normal. The auricles were dilated; the inner walls were smooth. The aorta was free. There was no sclerosis. The liver was enlarged and showed an advanced nutmeg change. The spleen also was enlarged and there was chronic congestion of the kidneys.

Anatomical Diagnosis: Acute vegetative endocarditis, (no bacteria), chronic congestion of the lungs, liver, spleen and kidneys.

Electrocardiographic Studies (Fig. 2). Several days before death the electrocardiogram showed a slight diphasic curving of the *T* wave in Lead III. The ascending arm of *QRS* was thickened in Lead I and finely notched in Lead III. Just before the patient died, the first evidence in the electrocardiogram was failure of the sinus and of auricular activity and a complete assumption of control by the auriculoventricular node (*b*). Besides, it must be noted that there was variation in the height of *R* with irregularity in its rhythm (*c*). This continued with progressive but irregular slowing of the nodal rhythm. The *T* wave was inverted, and at times there were fibrillatory waves suggesting auricular action. The *T* wave

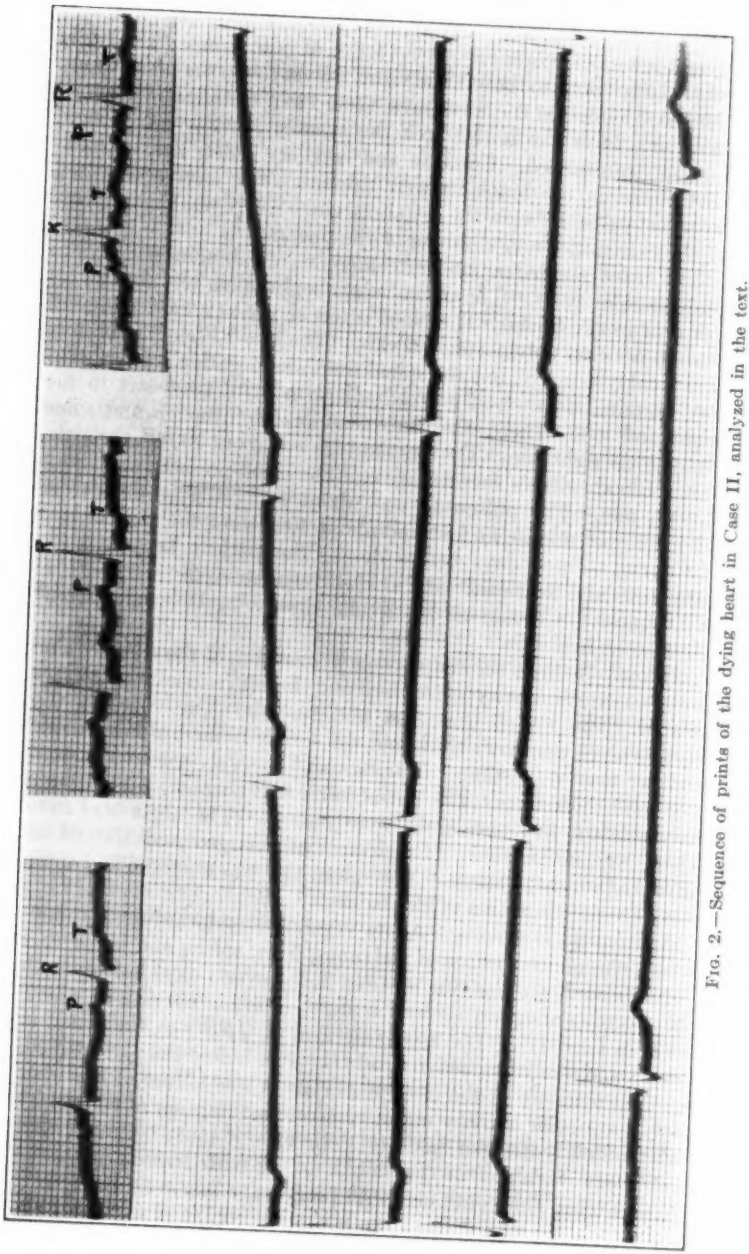

FIG. 2.—Sequence of prints of the dying heart in Case II, analyzed in the text.

gradually showed less inversion and more of an upright phase and finally became entirely upright (*d*). The *S–T* phase became slightly prolonged. After a very marked slowing, the last three or four ventricular beats showed distinct alteration in the contour of *S* (*e*). The interval between the last and penultimate beats was about ten seconds. About thirty seconds after the last beat, several peculiar movements of the string occurred, evidencing final ventricular contraction of extraordinary form.

Summary and Discussion of Case II. The sequence of events in this case may be summarized as follows: (1) Early failure of the atrial node without recovery; (2) nodal control with irregular rhythm; (3) progressive nodal slowing; (4) prolongation of the *S–T* phase; (5) change in direction of the *T* wave.

That pulsus alternans bears a close relation to the force developed by the ventricular contraction is well known. That is why it is of great clinical significance. This alternation of energy of the ventricular contractions produces a pulse in which the alternate beats are of lower amplitude. The electrocardiogram may indicate this alternation as well as the pulse-wave. (Fig. 2*c*).

Pulsus alternans also bears a direct relation to the changes in pressure in the left ventricle and in the arterial circulation. The amplitude of the pulse-wave is determined essentially by the capacity of contraction of the heart, that is, by the quantity of blood driven out into the aorta by the left ventricle during systole. This quantity depends upon the amount of filling of the left ventricle before systole, the pressure in the ventricle, and third the pressure in the aorta.

Pulsus alternans is therefore to be explained in many instances by the fact that the force of the ventricle can overcome a certain amount of aortic pressure. When, after a complete contraction, the aortic pressure rises, the energy of the next heart beat is partly utilized in overcoming some of this pressure before a pulse-wave becomes apparent. It is likely that both factors, the energy of systole which is primary in the muscle and the influence of arterial pressure, are the causes of alternation in a feeble heart muscle.[17] Vagus stimulation may abolish alternation by reducing the rate of the heart.[18]

Case III.—B. K., aged fifty-four years, was observed as a case of cardiorenal disease.

The patient had suffered from frequent attacks of tonsillitis. He had had a chancre at the age of twenty-one and scotomata and headaches for years. His last illness began rapidly seven months before death with swelling of the face and extremities and ascites. He had dyspnea and frequent vomiting.

[17] Dasbach: Onderzoekingen Physiol. Lab. Einthoven, Leiden, 1922, p. 118.
[18] Rihl: Ztschr. f. exper. Path. u. Therap., 1912, **10**, 8.

Physical examination showed pasty pallor, dyspnea, ascites and anasarca. His chest was emphysematous. The heart apex-beat was not visible and its sounds were weak and distant. The extremities were extremely edematous. The blood-pressure was 130/105 mm.

The urine showed a large amount of albumin and many hyalin and granular casts. The blood showed a slight secondary anemia. The blood Wassermann test was negative. The temperature on admission was normal.

Course: The abdomen was tapped of 2500 cc of colorless fluid, the examination of which showed: Cytology 10 cells per c.mm., 10 per cent polymorphonuclears and 90 per cent lymphocytes. After the tapping, the patient had a chill and the temperature rose to 103° F. The pulse became weak and irregular. He died with pulmonary edema several days after.

Diagnosis: Chronic cardionephritis.

Electrocardiographic Studies (Fig. 3). Before the patient died, the heart-rate was 90 per minute and gradually with slight variation in its slowing, it fell to 50 beats per minute. The *P* wave was very slight. The *QRS* wave was minute in Lead III, consisting of a diphasic wave directed chiefly downward and then upward, 1 mm. above and 1 mm. below the abscissa level. The *T* wave became inverted in Lead II after the rate slowed.

The last record was taken in Lead II after the patient was clinically dead. No heart sounds were audible and the peripheral circulation had apparently stopped. The record begins with a normal *P–R–T* sequence and a rate of 60 per minute. There is distinct sinus arrhythmia with slowing at times to the rate of 50 per minute. *P* is upright and slight. The *P–R* interval is at first 0.22 second and gradually increases to 0.4 second toward the end of this strip of record.

The ventricular complex changes as the heart failure progresses. It is upright and slight and the descending arm thickens as it descends. With the progress of failure, *S* terminates more and more above the isoelectric level and continues horizontally into an inverted *T*. The *T* wave tends to become inverted at first and later progressively isoelectric. One early ventricular extrasystole is noted arising from the base of the heart. (No. 103–2).

The record was continued in Lead II, but the amplitude of the string was doubled. (No. 104). The auriculoventricular node has assumed control. There is complete dissociation between the auricles and ventricles. The auricular rate is about 45 per minute while the ventricular is about 38. The *QRS* wave has become extremely widened. After the first few cycles *T* is no longer to be seen. There is progressive sinus slowing and marked nodal slowing. Momentary ventricular fibrillation occurs with temporary recovery. (No. 104–11). The last ventricular beat is followed by auricular

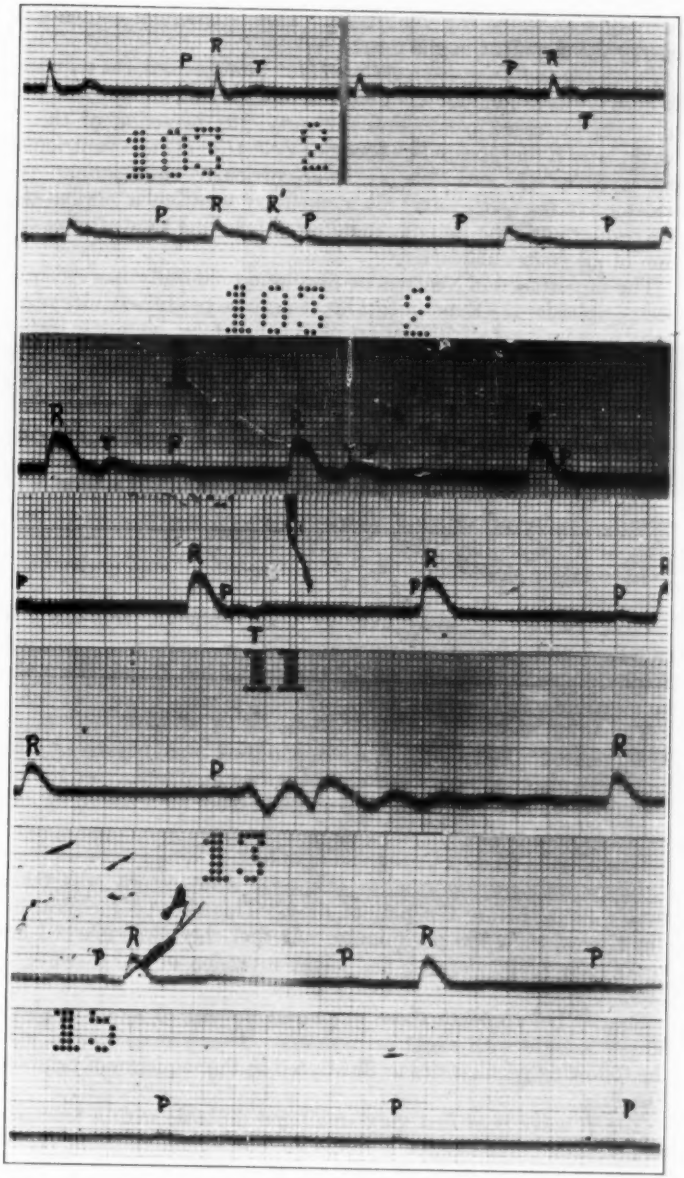

FIG. 3.—Sequence of prints of the dying heart in Case III, analyzed in the text.

activity manifested for some time. This is the final evidence of energy development in the heart.

Summary and Discussion of Case III. Summarized, the sequence of events was as follows: (1) Progressive sinus slowing and arrhythmia; (2) increased conduction difficulty; (3) inversion of the *T* wave; later it disappeared or became isoelectric; (4) one ventricular extrasystole; (5) complete auriculoventricular dissociation; (6) widening of the *QRS* wave; (7) momentary ventricular fibrillation; (8) regular auricular activity manifested for some time after cessation of all ventricular activity.

The importance of ventricular fibrillation clinically has recently been emphasized. Experimentally, it may be produced quite regularly in advanced digitalization of the heart by warming rather limited portions of the ventricle. Under digitalis the ventricle tends to assume independent automaticity and localized warming of the musculature produces a marked increase in the irritability of that part. Upon cessation of the warming, feeble irregular contractions or coarse undulations may occur.[19]

Ventricular fibrillation is a terminal phenomenon. One case is recorded, however, in which the heart recovered for a short time after ventricular fibrillation was shown by the electrocardiogram to have taken place.[20]

Case IV.—F. E., aged sixty-six years, suffered from diabetic gangrene and general arteriosclerosis. The heart was negative. Soon after admission and toward the end of her illness, there was no glycosuria and no acidosis.

The urine showed a moderate amount of albumin and many hyalin casts. The blood Wassermann test was negative. The blood chemistry showed an excess of creatinin, 3.1 mg. per 100 cc.

Course: The temperature was normal except for a rise to 105° F. with terminal coma.

Diagnosis: Diabetes, gangrene right foot, general arteriosclerosis.

Electrocardiographic Studies (Fig. 4). One record was taken twelve hours before the patient died. This showed tachycardia, slightly less than 150 per minute. At first there was marked left ventricular preponderance and slight inversion of the *T* wave in Lead I.

Shortly before death there was atrial slowing to a rate of about 60 per minute with slight arrhythmia. This was associated with the following peculiarities as illustrated in the sequence of prints in Fig. 4.

The *P* wave is at first very small and diphasic with a tendency to inversion. Its absence is frequent showing intermittent failure

[19] Schlomovitz: Am. Jour. Physiol., 1921, **55**, 485.
[20] Robinson and Bredeck: Arch. Int. Med., 1917, **20**, 725.

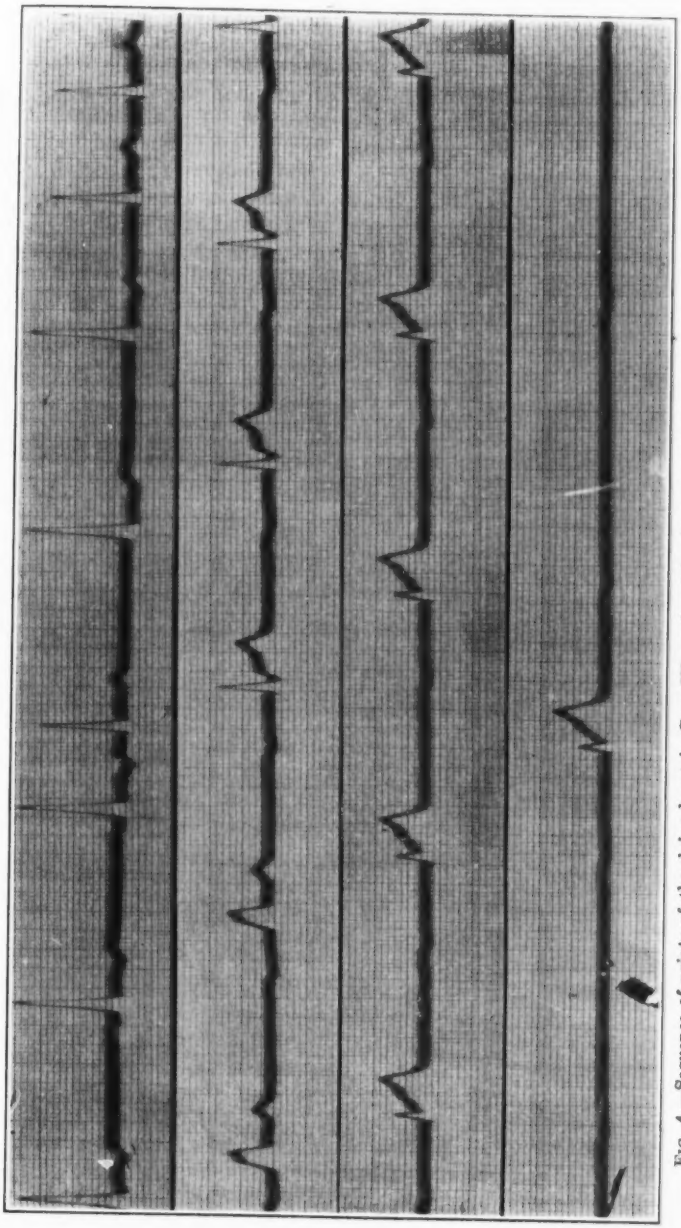

FIG. 4.—Sequence of prints of the dying heart in Case IV, analyzed in the text. Abscissæ 1 division = 0.02 second. Ordinates 1 division = 10^{-4} volts.

of the sinus node. When it does occur, it is followed without any impairment of P–R conduction by a ventricular cycle. The ventricular cycles occur in two distinct forms. One is higher in voltage and wider than the other. In this cycle, the T wave is diphasic, its first and main portion sharply inverted (*a*). This larger form of wave changes rapidly and becomes lower in amplitude and wider with marked notching and thickening and finally disappears (*b*).

Before this happens, however, its T wave has become upright. The other form which appears more normal and occurs with about equal frequency and irregularity at first, takes place occasionally also in response to a sinus stimulus. It gradually diminishes in voltage while its upright T wave increases in height. This last form of curve makes up all the ventricular cycles of the last portion of the record.

Conduction defect increases after the sinus has recovered, to a P–R interval of 0.45 second. Finally there is complete auriculoventricular dissociation. The last ventricular cycle is seen in strip *d*. After that auricular impulses are visible for several minutes at a regular rate of about 43 per minute.

Summary of Case IV. The sequence of events was as follows: (1) Sinus failure; (2) impaired or abnormal intraventricular conduction of many of the ventricular beats; (3) recovery of the atrial node; (4) progressive conduction defect; (5) complete auriculoventricular dissociation and (6) terminal auricular activity after the last ventricular cycle.

CASE V.—A. F., aged twenty-seven years, was a case of epidemic encephalitis.

The patient's last illness began five weeks before her death with severe continuous frontal headaches and abdominal cramps. She was feverish and dizzy when moving about with diplopia and drowsiness. At times, she spoke irrationally.

Physical examination showed ptosis of the right upper eyelid. The pupils did not react to light. The heart was not enlarged and there were no murmurs.

The urine showed a moderate amount of albumin and no casts. The Wassermann test was negative both in the blood and spinal fluid. The temperature was 100° to 101° F. throughout.

Course: Several days before death, the patient lapsed into coma and developed left hemiplegia. She died with marked cyanosis and cardiac failure.

Diagnosis: Epidemic encephalitis.

Electrocardiographic Studies (Figs. 5 and 6). The routine electrocardiogram in this case showed tachycardia with a rate of 150 per minute, left ventricular preponderance and high P and T waves in Lead II. The S–T phase exhibited what is probably a marked respiratory effect.

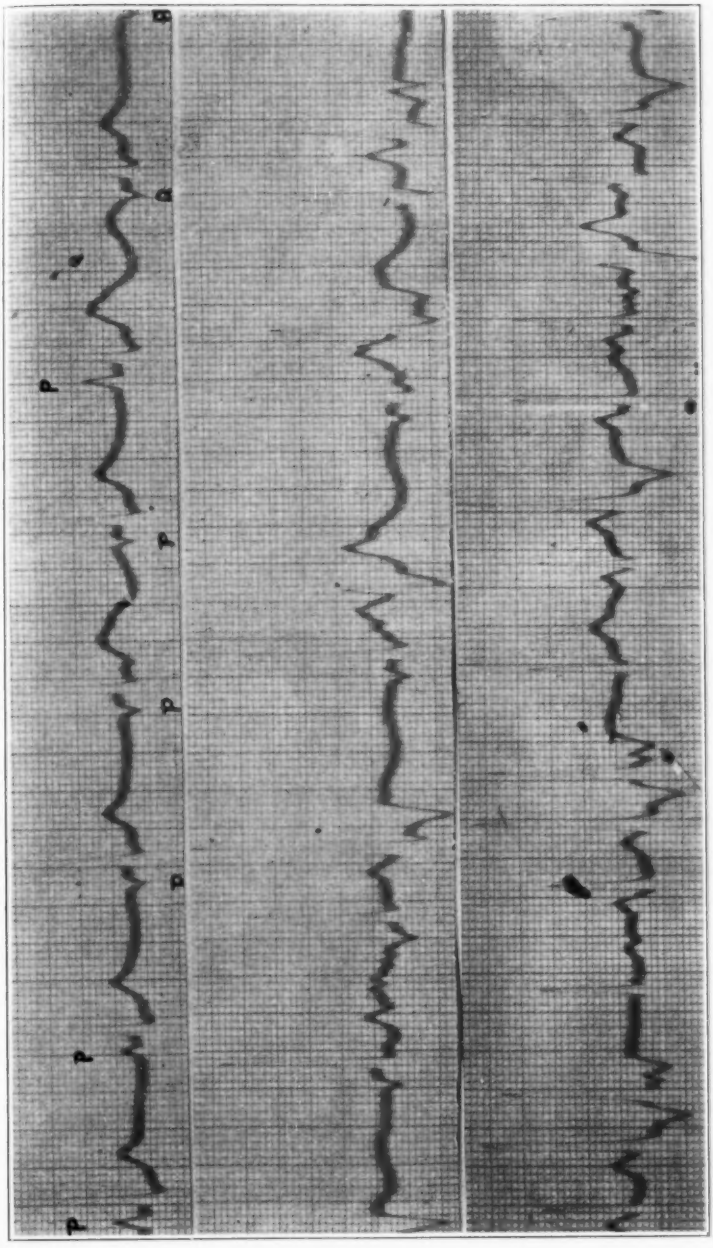

FIG. 5.—Sequence of prints of the dying heart in case V, analyzed in the text.

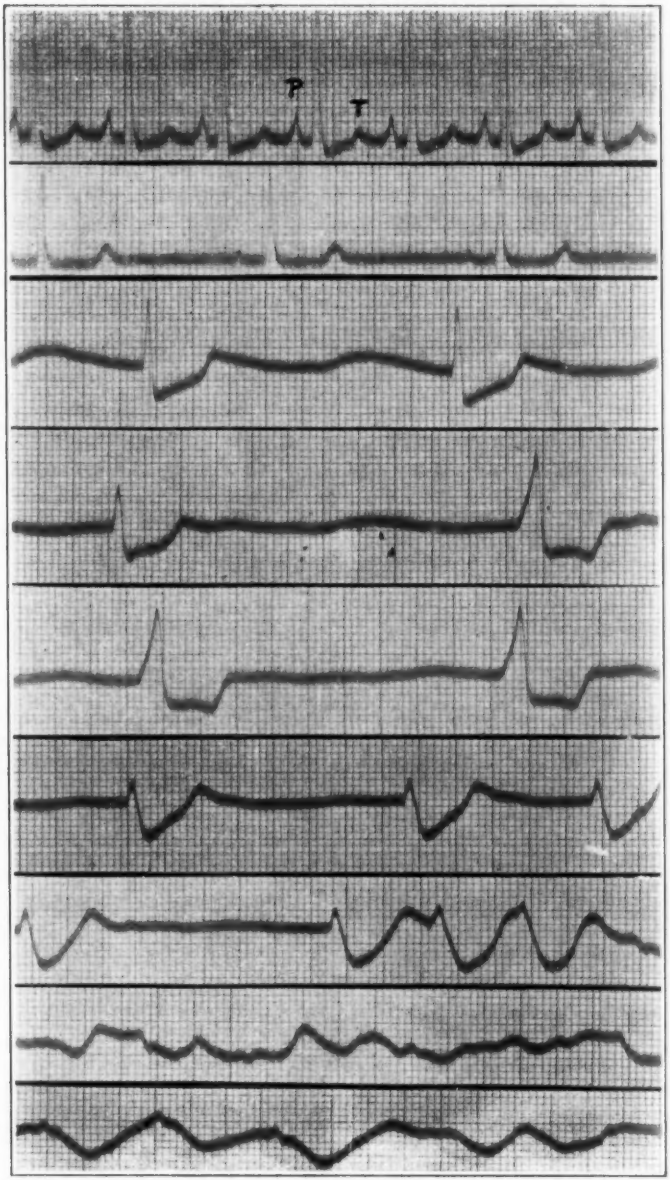

FIG. 6.—Sequence of prints of the dying heart in Case V, analyzed in the text.

The atrial slowing later became more marked. The *P* wave also became more acute. Suddenly, in one cycle, its amplitude diminished; then followed a remarkable inversion of the *P* wave for three cycles. The normal *P* wave recurred once, after which it was replaced by the inverted type of curve. The *P–R* interval, however, remained the same. This is quite remarkable and demands some discussion (Fig. 5*a*).

As the record progressed, however, nodal rhythm and nodal tachysystole became marked. Frequent ventricular extrasystoles of various types arising from various parts of the heart interrupted the record at every few cycles (Fig. 5*b–c*). These show no complete compensatory pause.

After a time, the normal form of the *P* wave with its previous *P–R* interval was again seen (Fig. 6*a*). The normal sinus rhythm without any extrasystoles returned and it is with this type of mechanism that the heart progressively died. This is shown in Fig. 6 taken in Lead II.

The sinus rate is slow, 50 per minute, with a *P–R* interval of 0.16 second and a small normal appearing *T* wave (Fig. 6*b*). Suddenly the *P* wave becomes prolonged and undulating, extending over a period of about 0.6 second, followed by an upright *QRS* wave with an abnormal *S–T* phase (Fig. 6*c*).

The long undulating *P* wave gradually becomes inverted, and then again returns to an upward curve but with much greater prolongation of the *P–R* period. The auriculoventricular interval is now more than one second (Fig. 6*d*). Suddenly the *QRS* wave becomes much widened; the *T* wave becomes inverted (Fig. 6*d*), and gradually the amplitude of *QRS* diminishes and complete dissociation of the auricles and the ventricles takes place (Fig. 6*f*).

After much nodal depression or slowing, the ventricle suddenly goes into fibrillation (Fig. 6*g*). For a period, however, waves occur with more or less regularity, at times slower and at times faster having a contour of terminal ventricular curves observed in other cases. After the last distinct ventricular wave, there is a prolonged isoelectric period after which there is a sudden irregular sequence of waves for several seconds terminating in the cessation of all heart action.

Summary and Discussion of Case V. Summarized, the sequence of events may be stated as follows: (1) Atrial slowing and sudden inversion of the *P* wave; (2) frequent ventricular extrasystoles of various types; (3) nodal rhythm and nodal tachysystole with frequent extrasystoles; (4) loss of sinus control; (5) recovery of sinus control; (6) atrial slowing; (7) rare form of *P* wave with extreme conduction defect; (8) change of *QRS* wave to abnormal widening; (9) deformity of *T* wave; (10) ventricular fibrillation; (11) partial ventricular recovery; (12) terminal fibrillatory waves.

Inversion of the *P* wave, which is strikingly seen in the first strip of Fig. 5, demands some discussion. Analyzing our data, we see first a high pointed *P* wave with a *P–R* interval of 0.12 of a second. This interval is not appreciably changed in any of the succeeding abnormal *P* waves, which would mean that the pacemaker was located in the sinus region. What is it then, that causes the inversion of the auricular wave?

We know that due to vagus influences, the form and height of the *P* wave may be changed. It may become negative, diphasic or small. These changes, it is also known, are not synchronous with changes in the ventricular curves. They are also not synchronous with inspiration and expiration.[1] It is upon this basis that the only explanation is forthcoming. This is especially the case as there are other manifestations in this electrocardiographic record that indicate vagal influence.

The contour of the *T* wave as is well known bears a close relation to the change in the direction of the conduction stimulus. This is illustrated especially in strip *d* of Fig. 6. In this strip, the first cycle is of one form and the second is of another form, in which conduction defect and inversion of the *T* wave has developed.

The rare abnormality and deformity of the *P* wave which takes place in strips *c–d* of the record requires explanation. A slow undulation, extending over a period of 0.6 second and bearing a regular relation to the ventricle, must necessarily be explained as due to auricular activity. It occurs with regularity in definite relation to the *QRS* wave. The *P–R* interval increases progressively. It is probable that both the abnormal wave and the increasing block are due also to vagal influence.

Case VI.—J. V., aged seventy-five years, was ill with bronchopneumonia one week before he died.

Physical examination revealed distant heart sounds of poor quality. The lungs were emphysematous and there was bronchopneumonia of the right lower lobe.

Course: The temperature was 101° F.; the terminal temperature was 100° F. The patient died with pulmonary edema.

Diagnosis: Bronchopneumonia.

Electrocardiographic Studies. Just before the patient died, the electrocardiogram showed left ventricular preponderance. The *P* wave was high. The *QRS* wave was notched at the apex in Lead II and in the ascending limb of Lead III.

The dying heart showed a complete change of mechanism with sinus failure and entire absence of the auricular wave. Later it returned, but in a very peculiar form. There was a slow, rounded curve of low amplitude and delay in conduction of 0.4 second. A short period later, the dissociation was complete. Fibrillatory waves

[1] Einthoven, Fahr and De Waart: Arch. f. Physiol., 1913, **150**, 275.

occurred at the end after the last ventricular contraction. Throughout the terminal part of the record, the ventricular curve is bizarre (Fig. 7).

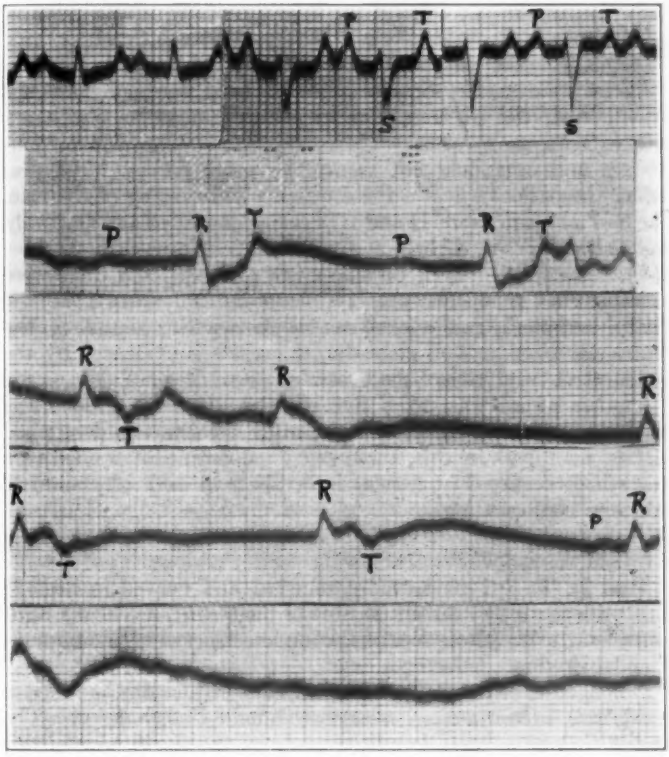

FIG. 7.—Sequence of the prints of the dying heart in Case VI, analyzed in the text.

CASE VII.—F. L., aged sixty-three years. The patient had suffered for seventeen years from frequent attacks of tonsillitis and rheumatism. For two years prior to her death, she had dyspnea, palpitation, nasal hemorrhages, hemoptysis, cyanosis, swelling of the legs, polyuria and nycturia.

Physical examination revealed cyanosis, dyspnea and orthopnea. The heart action was irregular with a pulse deficit of 18. There was a diffuse apex impulse and a systolic thrill in the sixth space.

The first sound was impaired and the pulmonic second sound was accentuated. The liver edge was felt below the level of the umbilicus and there was marked edema of the extremities.

The urine showed a large amount of albumin and the blood a moderate secondary anemia. The temperature was normal.

Course: Right hydrothorax and increasing cardiac decompensation developed. Toward the end, the pulse became very weak and slow. Adrenalin, ℿxv, was given hypodermically fifteen minutes before death.

Diagnosis: Auricular fibrillation. Right hydrothorax.

Electrocardiographic Studies. About two weeks before the patient died, the electrocardiogram showed auricular fibrillation with extreme tachycardia. There was right ventricular preponderance and occasional left ventricular extrasystoles. Just preceding the patient's death, there was marked slowing of the rate. The $S-T$ phase in Leads II and III became depressed and markedly rounded and T was slightly above the isoelectric level in all three leads. The $QRS-T$ cycle became much prolonged and there were occasional left ventricular extrasystoles of the same form as before. That heart-block and auriculoventricular nodal control of the ventricular rhythm took place during periods is evidenced by the comparative regularity of the beats.

Another record was taken five minutes after the patient was considered clinically dead, that is, after the heart had stopped beating audibly. In this, three slight indeterminate waves were seen which occurred at regular intervals from each other and of indefinite conformation.

Summary and Discussion of Case VII. Summarized, the sequence of events was as follows: (1) Slowing of rate; (2) lowering of T wave in Lead I; (3) $S-T$ phase more rounded and curved in Lead II with prolongation of the entire time of the $QRS-T$ cycle and right ventricular extrasystole seen; (4) complete block with assumption of nodal rhythm.

Prolongation of the $S-T$ phase was evident and does not seem, in this case, to bear a direct relation to bundle branch defect. The studies that have heretofore been made on the significance of this prolongation indicate that the variation in the length of the $S-T$ interval is more dependent on cardiac rate than on any other factor. It is not a constant accompaniment of any other phenomena of the electrocardiogram.[21]

General Summary and Conclusions. Seven electrocardiographic studies of the dying heart are reported. Three of the cases died from heart disease and the other cases from other illnesses. One of the three presented auricular fibrillation during life.

In all the cases, the first and main effect was failure of the sinus control of the heart action, with assumption of control by the auriculoventricular node. This is without doubt the most significant

[21] Buchanan: Arch. Int. Med., 1921, **28**, 484.

phenomenon in terminal heart activity. It is also in correspondence with the significant findings under experimental conditions.

The cessation of the normal auricular contraction stimulus seems to be the critical phenomenon in the process of death. Before this happens, the sinus node shows irritability and depression in various sequences and degrees and it is probable that if the disturbance could be controlled before cessation of sinus function, recovery of the heart might occur. After this happens, it is known experimentally that the heart will not recover although reoxygenated.

The simultaneous control by two centers of the heart's rhythm is definitely a sign of poor prognosis. It signifies sufficient depression of the sinus control to permit the auriculoventricular node to dominate the rhythm.

From a functional standpoint, it is obvious that this must lead to serious impairment of the circulation. Simultaneous auricular and ventricular contractions will frequently take place. Inadequate filling of the ventricles is the inevitable result when auricular contractions occur without any relation to the ventricular beats. No possible functional adaptation can take place between the upper and lower chambers.

Although ventricular extrasystoles are a common occurrence in the dying heart under experimental conditions, they were encountered in only 2 of the cases here reported. In 1 of the cases, they existed long before death and in the other case they occurred suddenly from various points in the ventricular muscle just at the time vagus effects were most notable, suggesting vagus influence as the cause.

Of course, a functional defect in conduction throughout the ventricle is apparent in most instances; it is due either to dromotropic influence through the vagus depressing conduction, or to nutritional disturbances of the conducting mechanism.

Ventricular fibrillation occurred in 2 cases. In 1 instance, it was only momentary and in the other more prolonged. In both, this was followed by a very short period of recovery of rhythmic ventricular action, but without any regularity. The ventricles stopped beating before the auricles in 3 cases. In the other 3, auricular action ceased first. It is usual in the human dying heart that the electrocardiogram will continue to show evidence of activity without there being any visible or audible evidence of ventricular systole.

As a result of this study, we want to call attention to the greater importance of the earlier phenomena in the auricles as compared with those which occur later in the ventricles, when the conditions are beyond recovery. We say this in view of the findings in a large number of other cases to be reported in which the early criteria were used in a study of their prognostic significance.

The emphasis upon the earlier disturbances of auricular action

are important, since intracardiac injections of epinephrin and other stimulants may be of life-saving value and since it has not yet been ascertained in what period in the process of death of the heart their value may prove greatest.

In correlating our findings with those of the two or three previous clinical studies on this subject, we feel that one is justified in considering change in height, direction and contour of the S–T period and the T wave as the only change encountered in every case, but this is more or less of a very late phenomenon.

In 1 of our cases, the QRS wave (Fig. 2) underwent almost no alteration. The changes that did affect the QRS wave in some instances, that is, lowering of voltage and widening and notching, are explained on the basis of intraventricular conduction defect. The changes taking place in the T wave have thus far eluded positive interpretation.

We want to express our thanks to the attending physicans of Beth Israel Hospital for permission to study these cases. We also want to thank Mr. Nicolai Opolonick for his technical assistance.

THE SURGERY OF PULMONARY TUBERCULOSIS.*

By John Alexander, M.A., B.S., M.D.,
ANN ARBOR, MICHIGAN.

(*Continued from July and August*, 1924)

The following always use regional and local anesthesia: Jessen, Ranzi, Shivers (in 5 of 20 operations he was obliged to add gas or ether), A. Christensen (without morphin), Willy Meyer, Eloesser, Ochsner and H'Doubler. Stöcklin and Schreiber used it upon 98 of 100 patients. Bérard prefers a combination of regional-local anesthesia and light general narcosis with ethyl chloride or nitrous-oxide-oxygen for one-stage operation upon patients whose expectoration is less than 60 to 80 cc a day. If the expectoration exceeds this, or if the operation is to be performed in two stages, he tries to operate entirely under regional-local anesthesia.

Archibald, Welles, Hedblom and Gravesen prefer to combine novocain-adrenalin and light nitrous-oxide-oxygen anesthesias, as less of each is needed, and dangerous symptoms may be expected from neither. Shortle and Gekler, Riviere and Romanis, and Willard Smith prefer nitrous-oxide-oxygen alone.

Sauerbruck, Saugmann, Bull, Davies prefer ether alone if the daily amount of sputum is small, and general narcosis may be necessary if the patient is extremely apprehensive, or greatly frightened by hearing the ribs cut, or by a sensation of "tightening"

as the chest narrows. Sauerbruch thinks that ether contributes less toward shock than does local anesthesia.

In order to minimize the postoperative pain some surgeons interrupt the intercostal nerves as far posteriorly as possible. Davies, Eloesser and Hedblom inject a few drops of absolute alcohol into each nerve; Nyström crushes the nerves and injects alcohol. Jessen, Schreiber and Mühsam resect 1 to 2 cm. of each nerve, sometimes together with a section of the overlying periosteum. Sauerbruch resects 1 to 2 cm. of each nerve in those patients whose periosteum is thick and edematous, as he has learned that, otherwise, they are liable to suffer from intercostal neuralgia. For many months there is total anesthesia in the nerve distribution, and then gradual compensation takes place by an overgrowth of neighboring nerves. Paralysis of the abdominal wall on the operated side has not proven harmful, although, on theoretical grounds, it would seem that coughing would be less effective, and that the bulging permitted to the costal border might remove a valuable place of counter-pressure for the collapsed posterior chest wall.

IX. Sauerbruch's Extrapleural Paravertebral Thoracoplasty. This operation may be considered a compromise between the extensive resections of the old Brauer-Friedrich technic and the narrow, columnar resections of only the upper seven or eight ribs of the earliest Wilms operation. Although only short lengths of ribs are removed, the resections are so placed as to obtain relatively great lung compression, and the clinical results are better than with any other technic, except possibly Brauer's modification of it. When skilfully performed it causes little operative shock, and rarely upsets respiration or circulation, and the resulting deformity is slight. It is the technic, although sometimes slightly modified, that is being used throughout the world by surgeons of greatest experience.

Position on Operating Table. The patient lies on the better side with both thighs flexed; a cushion is placed under the loin, another beneath the thighs is held firmly with a strap to prevent the patient from slipping. The upper half of the table is raised 30°. If a patient is orthopneic he sits across the table and leans forward on the shoulders of an attendant. Saugmann always used the sitting posture; Bérard does when using local anesthesia.

Incision. Provided the upper lobe is the more diseased, ribs XI to V are removed first, through a hook-shaped incision which commences 6 cm. from the fourth vertebral spine and runs straight down to the tenth rib, when it curves forward to posterior axillary, or midaxillary line (see Figs. 6 and 14). Jessen finds that an incision making an angle of 120° at the tenth rib is more convenient than the Sauerbruch "Bogenschnitt." Ostermeyer recommends a large Z-shaped incision which cuts the pectorals and subclavius, and loosens the serratus magnus and the latissimus, on the grounds that

there is less hemorrhage and that there is better protection of nerves and vessels. I believe that any such advantages would be offset by the greater operative shock and exposure of larger raw surfaces to the danger of infection, and by the fact that more than a safe amount of local anesthetic would be necessary. Towels clipped to

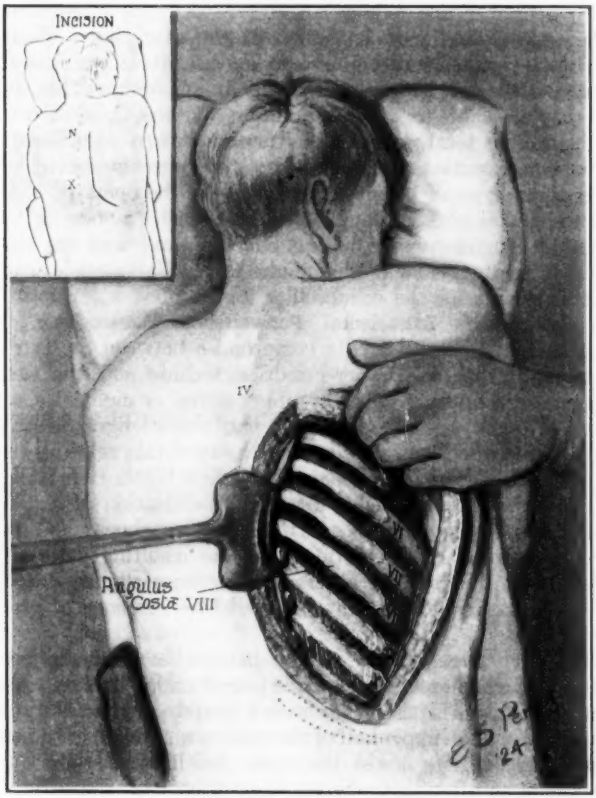

FIG. 6.—First stage of a Sauerbruch paravertebral thoracoplasty. The erector spinæ muscles have been detached from the angles to the necks of the ribs and retracted. Ribs XI to V inclusive have been stripped of their periosteum for the requisite distances; ribs XI, X and IX already have been resected. The scapula is being retracted by the hand.

the skin edges immediately after the skin incision is made constitute a wise precaution against wound infection.

After the lower ribs have been exposed they are best removed in this order X, IX, VIII, VII, VI, V, XI. If it is then decided to complete the operation, instead of dividing it into two stages, the

wound is packed with gauze and the incision continued straight up to the neck, and curved forward to the anterior edge of the trapezius. During the latter part of its course it will sever two medium-large arteries—branches of the suprascapular and of the transverse colli. Strong retraction in the angle of the wound affords an excellent view of the first rib. The upper four ribs are resected from below upward. The muscles and skin are sutured with interrupted stitches, using two layers for the heavy scapular muscles. A long rubber drain is inserted beneath the muscles, and emerges from the lower end of the incision.

In case the operation is divided into two stages it is not necessary to reopen, at the second operation, the incision originally made for resection of ribs XI to V. Incision for the second stage curves from the anterior edge of the trapezius down to the base of the neck posteriorly, 6 cm. distant from the vertebral spinous processes, and then runs vertically downward to the seventh rib, where it is made to curve forward around the angle of the scapula, thereby allowing the scapula to be displaced well forward to expose the ribs beneath it (see Figs. 7 and 14).

The ribs are usually removed subperiosteally. When pleura and periosteum are seen to be much thickened and inflamed, Sauerbruch removes the periosteum in order to prevent early regeneration of bone that would check the progressive narrowing of the chest that is expected to occur during many weeks, and also resects 1 to 2 cm. of the intercostal nerves to prevent postoperative neuralgia. Jacobaeus and Key and Nyström also remove the periosteum. Jessen favors rib regeneration as affording advantageous fixation of the chest wall; he removes rib sections at operation long enou h to make secondary narrowing of the chest unnecessary; he does not section the nerves as they are important for the nourishment of the tissues and for the stability of the weakened chest wall. Bérard fears that resection of the periosteum might complicate the operation by wounding the pleura, intercostal vessels and nerves. As prophylaxis against deformity Hug urges that great care be taken of the motor nerves, and of the erector spinæ and latissimus dorsii and trapezius muscles, as avoidance of kyphoscoliosis is largely dependent upon their strength and function.

Unless the ribs are very close together it may be found convenient to strip each rib of its periosteum before removing any of them; if this is done, gauze should be tucked beneath the ribs in order to steady the freed lung which is seen moving rather violently with respiration, but in a paradoxical sense, beneath the bare ribs (Welles).

The skill employed in resecting the ribs largely determines the time consumed by the operation, the amount of operative shock and postoperative pain. A longitudinal incision is made in the periosteum, which is then readily pushed away from the lateral

flat surface of the rib with a gauze sponge or ordinary periosteal elevator. At both the upper and lower edges of the rib, under the attachments of the intercostal muscles, the periosteum is usually toughly adherent, and its detachment with the commonplace elevators is time-consuming, and unless done with due care, may

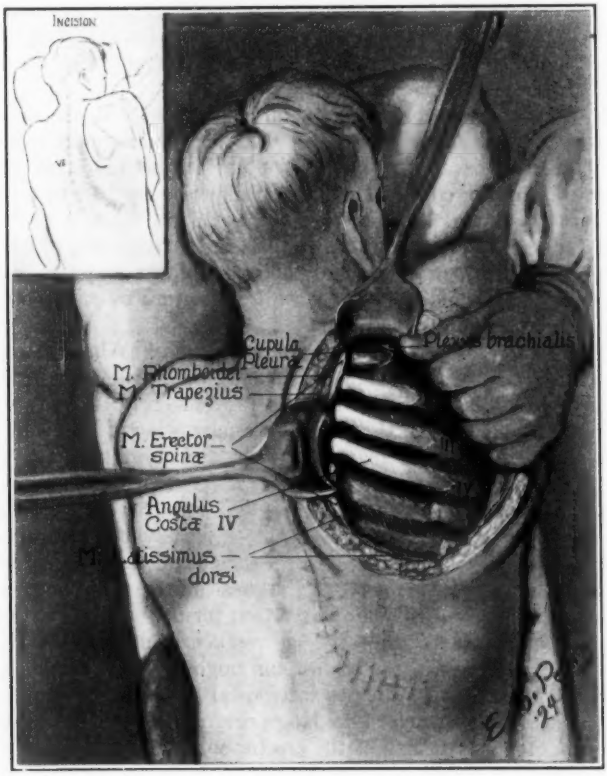

FIG. 7.—Second stage of a Sauerbruch paravertebral thoracoplasty. Ribs IV to I inclusive have been stripped of their periosteum for the requisite distances, and are about to be resected from below upward. The stumps of ribs V and VI, which were resected during the first stage of the operation, appear in the bed of the scapula.

tear the pleura. It should be remembered that its detachment here is somewhat simplified if the surgeon always works from before backward on the lower rib edge, and from behind forward on the upper rib edge. I have recently designed an instrument* that accomplishes this difficult step in thoracoplasty neatly and with

* Manufactured by George Tiemann & Co., 107 East 28th St., New York City.

very great saving of time, and without danger to the pleura. After the rib edges are freed of periosteum the Doyen raspatory is used to separate the periosteum from the posterior surface of the rib. The freeing of the rib posterior to its angle may prove very difficult, as here it is covered with the tough attachments of the erector spinæ muscles; it is best accomplished with a very sharp periosteal elevator, curved on the flat, this being used to cut and scrape away these attachments. Sauerbruch often removes the periosteum with the rib posterior to its angle, but takes care not to wound the pleura or intercostal vessels and nerve.

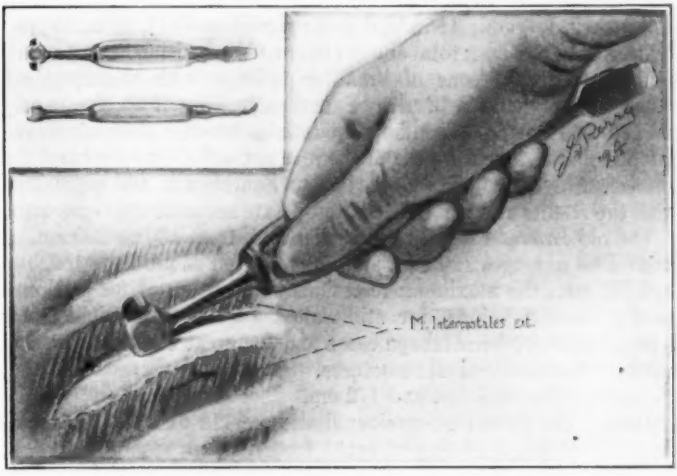

FIG. 8.—Author's rib-edge periosteum stripper in action.

The rib is sectioned with a rib shears, first anteriorly, then posteriorly (beneath the broad erector spinæ mass, which first must be dissected from the ribs), as near to the transverse process of the vertebra as possible. Saugmann recommends cutting the second and third ribs in their middles if they are very hard to reach, and then, by elevating each segment, the anterior and posterior sections may more easily be made. The double lever type of rib shears is much to be preferred to the commonplace ones which frequently cause fatigue-cramp of the surgeon's hand after two or three ribs have been cut. A special shears with a long neck is very convenient for the deep-lying first rib. As it is very difficult to resect the ribs as far as the transverse processes with these bulky instruments, it is frequently necessary to shorten the posterior stumps with rongeurs. Schreiber has at times removed parts of the transverse processes in an attempt to lessen the capacity of the costovertebral

gutter in order to obliterate large cavities. The distance between the vertebral bodies and the transverse processes is from 4 to 5 cm.

Sauerbruch's highly trained team's operating time is from ten to twelve minutes. He does not say whether this is for a complete operation or for one of two stages, but it does include the whole operation, from incision to skin suture. He believes that speed is an important factor in operations upon tuberculous persons. Jessen can do the complete operation, ribs XI to I, in twenty minutes. Bull's average time, with one or two assistants, is one hour. Either stage of the operation may be performed handily by a well-trained team in forty minutes.

Lengths of Ribs Resected. Sauerbruch's average resections are as follows: rib I, 3 cm.; II to V, 6 to 8 cm.; VI to VIII, 12 to 15 cm.; IX to XI, 12 to 6 cm.; total about 110 cm. While using Sauerbruch's technic, most surgeons of broad experience with thoracoplasty resect greater lengths of rib. Sauerbruch himself is frequently obliged to resort to secondary operations because the pulmonary compression obtained by the first one is not sufficient to control the disease. Shivers removes more rib than Sauerbruch, and is gratified with the results and rarely needs to operate secondarily.

The old Brauer-Friedrich operation took from 130 to 200 cm. of ribs. Bull averages 120 cm., and has removed as much as 150, 160 and 183 cm., the maximum resections being reserved for predominantly caseous lesions, for stiff-walled cavity or bronchiectatic types, for severe hemorrhage cases and for great traction displacements of the mediastinal structures. Saugmann averaged 134 cm., his limits being 80.5 cm. and 172 cm. Jacobaeus and Key average 140 cm. The Stöcklin-Schreiber limits are 110 and 140 cm., relatively great lengths being resected from the upper ribs according to the Brauer technic, which will be described below. Lorey has taken 175 and 180 cm. by the Brauer technic; Brauer himself averages only 125 cm.

The first rib must be resected, or at least divided, for efficient pulmonary compression, as the chest "hangs" on it; it is, as Bérard says "the key to the thoracic dome," the settling of the whole hemithorax that follows its section is practically necessary for the obliteration of apical cavities. Surgeons are almost unanimous about this. Unfortunately it was the early practice of some surgeons to leave it untouched, because of the difficulties of reaching it, and the possible dangers of injuring the subclavian vessels and the brachial plexus, which are in intimate proximity with the rib. It may be left intact only when the apex is so shrunken as to have sunk beneath it to the second rib (Sauerbruch; Madinier); or, as Bull says in opposition to Sauerbruch, if the apex is free of disease. If the first cartilage is very pliable, simple division may suffice; a 3 to 5 cm. resection of the posterior extremity is considered satisfactory; attempts to remove greater lengths threaten injury to the vessels and nerves.

The Eleventh Rib. Brauer and Saugmann see no advantage in resecting this rib. Bull, Sauerbruch, Baer and almost everyone else remove it for the reason that the diaphragm thereby loses some of its bony support and rises into the chest and assists in compression of the lung; also diaphragmatic movement is somewhat impaired and this adds to the pulmonary rest.

The Clavicle. Twelve years ago Wilms occasionally removed a small section of the clavicle to allow the weight of the shoulder to assist in the compression. More recently Eloesser has resected from 2 to 8 cm. and sutured the Z-shaped incision in the bone with kangaroo tendon. This procedure has not gained favor because it causes considerable deformity, and because it has not been shown to be particularly efficacious; the weight of the shoulder tends to fall forward rather than inward.

Interruption of Operation. The question as to whether complete thoracoplasty should be performed in one or several stages has been much debated. It should be recalled that, in any event, the less diseased lobe must be operated upon first in order to prevent aspiration when the secretion producing lesions are compressed. While agreeing with this, Brauer calls attention to the fact that this order of operating does not absolutely assure against aspiration.

The advantages of the two-stage operation are: (1) Less shock and less sudden changes demanded of the circulatory and respiratory mechanisms, which are enabled to adjust themselves gradually. Since Jessen has been using two stages he no longer sees the acute disturbances of circulation and respiration, and no longer is forced to use stimulants. Bérard favors the one-stage operation; he has been fortunate in having had no immediate operative deaths; his patients, however, experience two or three very stormy and dramatic postoperative days; great pain and dyspnea and difficulty in expectorating, cyanosis, high pulse and temperature, and sometimes anginoid or asphyxial attacks as a result of mediastinal displacement. (2) Fewer toxic products are pressed into the general circulation to endanger latent lesions in the better lung; therefore two stages are important if the better lung is under suspicion of activity. (3) The first stage usually causes enough rest and relaxation of the lesions to bring about a definite clinical improvement, which betters the chances of success of the second stage. Nine of 36 of Schreiber's patients were distinctly improved during the two or three weeks following the first stage, and two of them, one with a cavity, became entirely cured without necessity for the rest of the operation! Jessen speaks of the marked improvement in general condition, and in some cases in lesions of the better apex, following the first stage.

The advantages of the one-stage operation are: (1) Much preferred by the patient. (2) Risks of embolus, and anesthetic poisoning, and of wound infection run only once. (3) If wound infection should occur the whole lung has been compressed – no need to post-

pone a final stage of the operation. (4) Muscles are sectioned only once. (5) More even lung compression, and so less irritation of cavities and fewer chances of lung hemorrhage. The scapula fits more evenly against the lung (Gravesen).

It follows that every case is a law unto itself, and that it may be found advisable to interrupt an operation that was commenced with the intention of completing in one sitting. Hauke reports a one-stage operation during which the patient's condition was excellent and did not suggest interruption of operation; twelve hours later came paradoxical respiration, dyspnea, cyanosis and small pulse. It is important to realize that it is usual for the pulse to be 120 or more, and the respiration 40, during any thoracoplasty operation.

Statistics are hugely in favor of the two-stage operation; in Sauerbruch's earlier series there were 169 one-stage operations, with 2 operative deaths, and 21 deaths within the first three weeks, a total mortality of 13.6 per cent; there were 154 two-stage operations with 1 operative death and 5 others in the first three weeks, a total mortality of 3.9 per cent. In his later series there were 5 deaths (27 per cent) among 19 one-stage operations, and 2 deaths (4.2 per cent) among 47 two-stage operations. Stöcklin reports 9 operative deaths (28.1 per cent) among 32 one-stage cases, and 9 operative deaths (31 per cent) among 29 two-stage cases: it may be suggested that it is probable that the patients subjected to the two-stage operation were far sicker than the others, and that this may account for the fact that the figures of this series demonstrate no advantage for two stages. Jacobaeus and Key, Jessen, Ranzi, Welles and many others use two stages exclusively. It may be said in brief that there is widespread preference for the two-stage operation, but that one stage may be preferable if the patient is in excellent general condition, if the mediastinum is well fixed to prevent undue displacement of heart and trachea, and if the surgeon's technic is sure and rapid—a combination of circumstances that is met with very rarely.

Interval Between Stages. In the average case there is regeneration of rib from the remaining periosteum, often with bony bridging between ribs and with rigid fixation of the chest wall, six to eight weeks after operation. As stated above, some surgeons remove the periosteum to prevent this. If it does not occur, maximum retraction of the chest is not reached for nine months. It is clear that it is of great advantage to complete the second stage before bone regeneration occurs, because the progressive retractions of the upper and lower chest are reciprocally helpful and a rigid bulging of the one hinders maximum retraction of the other. It follows then, the patient's condition permitting, that the second stage should be done within six weeks of the first. Most surgeons give the interval as from two to three weeks; Davies says ten to fourteen days; Ochsner and H'Doubler, not more than six weeks. Sauerbruch says at

least two or three weeks. If the patient's condition has necessitated postponement of the second stage until new rib formation has occurred (Archibald recommends waiting six to twelve months if in doubt) it may be necessary, at the second operation, to remove some of this bone with chisel and mallet or with rongeurs.

Sauerbruch, Wilms, Brauer and Eloesser consider a partial large artificial pneumothorax over the less diseased lobe, followed by a partial thoracoplasty over the more diseased, adherent lobe, an absolutely ideal procedure. Tuffier and Eizaguirre prefer to use pneumolysis instead of partial thoracoplasty, in conjunction with partial pneumothorax. With either technic only one surgical operation is necessary, the diseased parts are permanently compressed, and the less diseased part of the lung resumes function when the pneumothorax is finally released. This combined pneumothorax-thoracoplasty is far safer than attempts to produce a complete pneumothorax by stretching adhesions with high intrapleural gas pressures.

Sauerbruch has now used this technic wherever possible for ten years, and has had splendid results, as has Stöcklin with 30 cases. As it is usual for the greatest disease and the most extensive pleural adhesions to be in the upper chest, artificial pneumothorax is usually induced below; this accustoms the heart and respiration to new conditions, and militates against aspiration when the partial thoracoplasty is done. Three weeks later, or when the intrapleural pressure is zero or slightly minus, ribs VII to I inclusive are resected by the paravertebral route. If the intrapleural pressure is then found to be too great it may be reduced by withdrawing gas from the pneumothorax. Great care must be taken not to wound the pleura when resecting the ribs that overlie the upper limits of the pneumothorax; if this occurs effusion and subsequently empyema are very liable to develop. In case the worse lesions were below and the pneumothorax partial above, the lower five or seven ribs would be resected.

The partial pneumothorax should be maintained for at least one year, if for no other reason than to prevent the grossly diseased part of the lung from slipping away from the compression of the overlying thoracoplasty. If the pneumothorax should be "lost" and adhesions form and compression of that part still be needed, completion of the thoracoplasty would be indicated. If both upper and lower lobes were severely diseased at the time of operation Jessen and Gravesen would prefer the permanent action of a total thoracoplasty to a combination of partial thoracoplasty and partial pneumothorax.

It happens sometimes that the Sauerbruch operations described above do not produce sufficient compression and rest to control the disease. Some supplementary operation then becomes necessary. Parts of the upper cartilages and anterior ribs (I to IV, or as many

as I to VIII) may be removed through a parasternal incision, as Wilms used to do routinely, and as Sauerbruch, Bérard and others do now. Phrenicotomy may be done, but this is more commonly performed as a preliminary to the first thoracoplasty. Pneumolysis is the supplementary operation of choice in a great majority of cases.

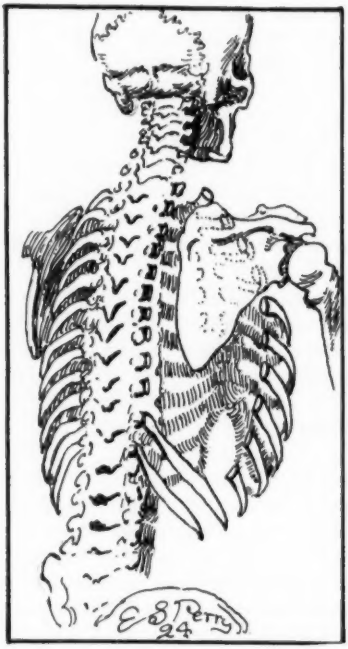

FIG. 9.—Extent of rib resection in Brauer's subscapular paravertebral thoracoplasty. The scapula falls against the upper lung and aids in compressing it.

X. Brauer's Subscapular Extrapleural Paravertebral Thoracoplasty

This operation differs in no way from the typical Sauerbruch operation, except that it resects greater lengths of ribs from beneath the scapula, allowing it to fall in on the lung and exert maximum pressure over the seat of maximum disease. Brauer has used this technic since 1911, and is greatly pleased with his results. It is his belief that in severe disease the results are directly proportional to the amount of lung compression, and that in many cases the compression obtained by the Wilms and Sauerbruch operations is insufficient. Stöcklin and Schreiber, Bull, Lorey, Jacobaeus and Key incline toward the Brauer technic.

Brauer does not remove the XI rib, nor the I if the apex has retracted below it. His average resections are: X, 10 to 13 cm.;

IX, 12 to 16 cm.; VIII to V, 15 cm.; IV, 13.5 cm.; III, 12.8 cm.; II, 8.8 cm.; I, 3.5 cm.; total 125 cm. To facilitate removal of the ribs lying under the axillary border of the scapula he sometimes makes a supplementary incision in the axilla. He aims to have the posterior cut rib-ends exactly even with one another. His plates show an even greater lung compression than obtained by the old Brauer-Friedrich operation. The shoulder does not descend much, movement of the arm is not impaired, there is little gross visible deformity, and yet there is maximum compression. The dangerous chest-wall flutter of the Brauer-Friedrich operation does not occur as ribs remain in the inferior anterolateral area of the chest which is but poorly protected by muscles against flutter.

Theoretical objection to the Brauer operation might be offered on the grounds that the arm and shoulder movements would tend to tug at and irritate the lung upon which the scapula rested, and to which it was adherent, and that this would tend to activate the tuberculous lesions. Adams has reported a case of chronic, non-tuberculous empyema cavity in which a somewhat similar operation was used with the result that the arm movements, transmitted to the lung by way of the scapula, caused the collapsed lung to expand. However, Brauer's reported results are unsurpassed.

XI. Extrapleural Pneumolysis. Pneumolysis is the separation of a lung or a part of a lung, together with both its visceral and parietal pleuræ, from the ribs and chest wall. It effects relaxation or compression of the lung. The space created by the separation may be filled with various tissue grafts or tampons, or not filled at all. Pneumolysis is used as an independent procedure, or as concomitant with, or as supplementary to, a thoracoplasty. It is rarely used except for the upper lobe, and when limited to the apex is commonly termed "apicolysis." As it is only practical to separate the lung to a limited extent, it follows that the procedure is indicated only to compress circumscribed lesions—cavities and lesions especially at the very apex, which is relatively less compressible by the usual thoracoplasty than the rest of the lung. It may be able to control persistent hemorrhage.

Pneumolysis Concomitant with Thoracoplasty. As precaution against insufficient compression by thoracoplasty Bull, Shivers, Archibald, Stöcklin and Schreiber routinely perform apicolysis immediately after resecting the upper ribs. I believe that the mere freeing of the lung, without leaving the space thus created full of something more substantially compressing than air (unless frequently renewed) does not warrant the time consumed and the danger of tearing into infected pleural or lung tissue. The additional lung compression is lost as soon as the extrapleural space obliterates itself by absorption of its contained air.

Pneumolysis secondary to thoracoplasty is a very valuable procedure for cases whose lesions, usually stiff-walled cavities, have

not been sufficiently compressed by a thoracoplasty. As improvement and fibrous encapsulation may continue for from six to twelve months after thoracoplasty, at least six months should have elapsed before pneumolysis is advised. Incision for this supplementary operation may be made either anteriorly or laterally, but in many cases it is preferable to open the upper end of the former paravertebral incision, resect sections of the upper three or four ribs, if regeneration has occurred, and proceed to separate the lung from behind (Sauerbruch; Ranzi).

Pneumolysis as an Independent Procedure. This has the advantages and many disadvantages of all partial procedures, which have been discussed above under "choice of operation" (page 279). It has certain specific disadvantages that must be mentioned: (1) The danger of tearing into infected pleura or lung at operation is a real one; (2) "fills" or grafts used to fill the space created between lung and chest wall not infrequently cause infection and are extruded, sometimes through the incision, sometimes into a pulmonary cavity because of pressure necrosis of its wall (Sauerbruch saw this occur 3 times among 40 cases); (3) a large "fill" causes greater pressure upon the mediastinum than does a modern thoracoplasty, and sometimes the dyspnea and cardiac disturbance are so great as to demand removal of the "fill."

As an indepent procedure Sauerbruch thinks it indicated only where very localized tuberculosis is entirely inactive, and so shrunken as to demand release of tension; it is his opinion that if active disease, even when circumscribed, demands operation at all, it demands a more effective operation than pneumolysis alone. Tuffier, the originator of the operation, still believes that it is indicated for apical disease in preference to thoracoplasty, which he considers dangerous and complicated and should be reserved for cases with very extensive disease. That pneumolysis as an independent operation has effected many cures is indisputable; but that, everything considered, it is far inferior to total, or even partial thoracoplasty is a fair deduction from the evidence.

Technic. The anterior or axillary routes are used by all except Ranzi, Henschen and Sauerbruch, who prefer paravertebral incision on the grounds that it gives best access to the costovertebral gutter which they believe contains the most important part of the lung to free and compress—unless the cavity or worse lesions are far anterior; they further hold that a posterior "fill" is less liable to embarrass the mediastinum and great vessels, and that the thick muscles of the back afford the best protection against extrusion of a "fill." For the anterior route, incision is made in the direction of the fibers of the pectoralis major, and 3 to 4 cm. of the second, or second and third, or second, third and fourth ribs removed parasternally. For the axillary route a J-shaped incision is made over ribs III and IV, and 6 to 8 cm. of each resected, and excellent

opportunity is afforded for extensive pneumolysis (Bull). By the paravertebral route a few centimeters are removed from ribs II and III.

After the rib sections are removed, the parietal pleura is carefully exposed by splitting the intercostal muscles and endothoracic fascia, or by dividing with a knife in the vertical direction, the posterior rib periosteum and endothoracic fascia, which are normally adherent. Then with some blunt instrument, or better with the index finger, perhaps covered with gauze, the lung with both pleuræ adherent to it is very carefully separated from the chest wall. Great caution is needed to prevent tearing into superficial cavities or other lung lesions; it is important that the separating finger or instrument always work against the ribs and intercostal structures, rather than against the lung; it is safer to create a broad space before advancing, rather than to work in a long, narrow channel. It may be necessary to divide certain very tough adhesions with scissors or knife; in certain cases it is impossible to effect separation at all. The firmest adhesions are liable to be found over the vertebral bodies (Tuffier). To approach too near to the mediastinum, either anteriorly or posteriorly, is to expose it to the danger of acute infection, the germs being freed from latent foci in the pleura; Henschen has advised rubbing iodoform powder into the raw surfaces to counteract this danger. The endothoracic fascia is often not well defined, and no particular care need be exercised to commence the pleural separation internal to it, as it is soon torn through if separation is begun external to it. It is not advisable to use the interpleural space as the line of cleavage, as the danger of stirring up infection and of tearing into the lung is greater than if the separation be made external to both pleuræ. Sauerbruch and Roux-Berger warn against performing pneumolysis in the presence of a partial pneumothorax because of the danger of tearing into it; if this occurs the danger of a fatal empyema is great. Jessen and Ranzi, on the other hand, recommend a somewhat limited pneumolysis, after resection of a part of a single rib, directly over an adhesion that is preventing the full efficient action of an artificial pneumothorax and that is not suited for Jacobaeus' cauterization. Jessen uses no "fill;" Ranzi uses a fat graft, or "Humanol," a liquefied human fat. Jessen determines the exact position of the attachment of the adhesion to the chest wall with the roentgen-ray; Ranzi outlines its position by puncturing the chest wall with a needle and observing its distance from, and relation to the adhesion through a thoracoscope. These operations cannot be recommended.

Hemorrhage from the separated surfaces may usually be controlled with temporary packs. Henschen has used hydrogen peroxide; theoretically it is of questionable wisdom to permit contact of gas bubbles under pressure with open pleural veins, in view of the frequency with which air-embolus is believed to occur from the

pleura. No case of so-called pleural eclampsia has been reported as due to pneumolysis. If a pulmonary cavity should be torn into during the operation it should be packed with gauze, and nothing further done. If a thin cavity wall is known to be beneath the site of operation it may be wise to pack the extrapleural space for a few days, rather than to introduce a "fill" at once. If the pack does not cause spontaneous rupture of the cavity, the "fill" may safely be placed; if the cavity does rupture it should be packed and drained until it has filled with granulations (Sauerbruch).

"*Fills.*" Many methods have been devised to fill the extrapleural space. The following have been used: fresh or preserved grafts of omentum, lipomata, subcutaneous fat, fibroids, bone fragments; pedicled grafts of pectoral muscle; inflatable rubber bags; maintained extrapleural artificial pneumothorax; lumps of paraffine; gauze tampons. Of these, fat and pectoral grafts, paraffine and gauze tampons are the only ones extensively used at present. The colpeurynter-like bags of Gwerder and Jessen and the inflated rubber glove of Kroh are objectionable because infection of the raw surfaces is unavoidable. Gas from an extrapleural pneumothorax (A. Mayer) is too rapidly absorbed to make the method practicable, and early obliteration of the cavity by adhesions creeping from its limits is inevitable. Jessen has obtained some "results" by leaving part of his incision open to form a sinus between the extrapleural cavity and the skin; as the air pressure then remains the same in the cavity and in the trachea, the lung stays collapsed. He has used this technic only when artificial pneumothorax or thoracoplasty was impossible, or when he has created such a large extrapleural cavity that it was impracticable to fill it with grafts or paraffine. Four patients treated by Jessen in this manner died of aspiration pneumonia; he does not report the total number of operations.

Gauze Tampon "Fill" of Schlange and Sauerbruch. In 1907 Schlange filled a pneumolysis cavity with iodoform gauze for hemoptysis. Sauerbruch prefers the tampon "fill" to all others; he packs snugly for six to eight weeks, and then permits the remaining pocket to become filled with granulations, which obliterate it. If after separation of the pleuræ from the chest wall he thinks the pleuræ are too thick to "give" under moderate tampon pressure, he pares away some of their thickness, and then packs. Roux-Berger changes the gauze pack every five days. Jessen tampons tight for fourteen days, and then secondarily sutures the wound. Stöcklin much prefers a paraffine "fill" to temporary tamponade as he believes that the latter technic the granulations which obliterate the hole change to scar and must eventually stretch the lesions that had been compressed by the pressure of the tampon, and also pull open cavities whose walls may have been approximated.

Fat "Fill" of Tuffier. Tuffier was the first to perform pneumolysis (1891). In 1910 he "filled" with a piece of fresh human omentum, removed during another operation. In 1911 he used a fresh lipoma. He claims that these grafts become firm fibro-adipose tissue. Baer says that fat grafts become absorbed too fast for the lasting compression demanded for tuberculous lesions. Archibald says they are absorbed, or changed into fibrous tissue. Sometimes sterile effusions will form about these grafts, and, unless aspirated promptly, cause their extrusion. Tuffier is still using fat "fills," and since the War has had no accident or elimination. He no longer uses the Baer paraffine "fills" because he believes they are less well tolerated than living grafts, and because they are so frequently eliminated.

Bull has used fat grafts 12 times, but does not report his results. He now uses abdominal wall fat, together with the superficial fascia, in preference to fat from the thigh, as it is less stiff, and so molds itself better to the irregularities of the cavity. Morrison and Eliasberg also use fat grafts.

In 1914 Tuffier reported 10 clinical successes out of 15 cases; 4 grafts were eliminated; 2 patients died several months later from progression of disease on the originally better side. Jessen reported 6 improvements out of 6 cases, but five years later 4 of them were dead and 1 of the 2 living had a permanent sinus. Kalb reported 2 successes and 1 failure; Oeri, 3 successes; Ulrici, 1 improvement; Rieckenberg, 2 very good results; Wilms, 5 cases without any elimination. It should be mentioned that in these cases pneumolysis was used as an independent procedure (without thoracoplasty), and that the poor results may be explained upon the grounds that poor results are to be expected from any partial procedure.

Paraffine "Fill" of Baer (1913). Five or 10 gm. lumps of a mixture of paraffine with a melting point of 48 to 56° C., 0.5 per cent bismuth carbonate, 0.5 per cent iodoform are packed into the cavity with spatulæ and various sized spoons.* Jessen uses a mixture of wax and vaseline as it is lighter than Baer's mixture and is more slowly taken up by the tissues. Davies has recommended pouring in liquid paraffine, but Sauerbruch warns against this as it devitalizes the tissues.

There are two principal objections to the method: (1) Large, heavy masses may cause threatening mediastinal pressure symptoms requiring removal of the "fill." One case of Sauerbruch's developed cyanosis and orthopnea, and the "fill" needed to be removed and the extrapleural space lightly tamponed. Two other of his cases, having 1000 gm. and 1200 gm. "fills," developed some untoward symptoms, but not severe enough to demand removal of the "fills." Henschen,

* Further detail as to the technic of the operation may be found in a recent article by Baer: Plombierung bei Lungentuberkulose, München. med. Wchnschr., 1921, **68**, 1582.

on the other hand, once used 1800 gm. and made no mention of complications. (2) Paraffine "fills" are essentially foreign bodies in the tissue and as such are liable to be eliminated, whether infected or not. This occurred in 7 of Sauerbruch's 28 cases, but in none of Stöcklin and Schreiber's 13. C. Spengler lost 2 large "fills" (800 gm. and 1000 gm.), one rupturing into a pulmonary cavity, the other externally. Rivière and Romanis managed to retain one that threatened elimination by repeatedly aspirating the sterile effusion that bathed it; another of their "fills" was lost because another physician incised into the effusion instead of aspirating it. It has been learned that repeated aspirations of the sterile effusions which many paraffine "fills" excite will prevent elimination in a large majority of cases, provided aspiration is commenced as soon as fluid is demonstrable.

Good results with Baer's paraffine "fills" have been reported by Baer, Eiselsberg, S. Neumann, Kalb and Oeri. In 1921 Baer reported 4 cases of bilateral disease with cavity, greatly improved five to eight years after pneumolysis and paraffine "fill" on the worse side, and 2 other cases of unilateral disease greatly improved two and a half and three years after operation.

Ranzi has reported 10 Baer "fills" and 1 fat-muscle "fill" after pneumolysis. The fat-muscle case died on the twentieth postoperative day of mediastinitis consequent upon a tear into a pulmonary cavity. There were 4 other deaths (1 in ten months following rupture of the paraffine into a bronchus; 2 of tuberculosis; 1 of cause not given); 2 were worse at two years; 1 was improved at two years, and 3 much better, one and a quarter to two and a half years. The largest paraffine mass used weighed 350 gm. Kutscha-Lissberg used the Baer technic in 6 cases. Three died in from seven months to two years; 2 were greatly improved, and 1 was cured. He is now of the opinion that two of the patients who died, both with lesions of the apex and beyond, should have had total thoracoplasty. However, most of these and Ranzi's patients had involvement of only a part of one lobe, and it is almost indisputable that a total thoracoplasty would have furnished far better results than these.

Muscle "Fill" of Archibald. An oblique incision is made from about the midsternum to the deltoid, and most of the sternal and costal fibers of the pectoralis major, and if desired all of the pectoralis minor, are detached; this fashions a large graft with a pedicle at the acromiothoracic axis; or a pedicle may be left at the sternum. About 6 cm. of ribs II, III and IV are now resected parasternally, and pneumolysis performed; access may be difficult to the posterior inferior surface of the upper lobe. The muscle graft is now stuffed into the hole and tacked with a few catgut stitches to the periosteum. This method is a valuable one when used as supplementary to a primary thoracoplasty. The graft is almost certain to live, and the

function of the arm is but little impaired. It has the disadvantage of not offering a large enough "fill" where a relatively large extrapleural space has been created, or where the pectoral muscles are small in a thin subject. As minor modifications of this procedure I suggest: (1) An S-shaped incision in preference to a straight incision, or to the more complicated rectangular flap; this incision enables the surgeon easily to disinsert the lower fibers of the pectoralis major and affords better exposure of its upper-inner fibers; (2) inclusion of the superficial fascia and part of the subcutaneous fat in one piece with the pectoral graft in those cases where the surgeon expects to create a larger extrapleural hole than the usual pectoral graft could fill; (3) section of the internal and external anterior thoracic nerves as they enter the under surface of the pectorals. On theoretical grounds it is preferable that muscle adherent to a tuberculous lung be paralyzed rather than subject to active contractions; a possible objection to this suggestion is that the graft would lose volume owing to muscle atrophy.

Archibald and Shivers have occasionally pulled the graft backward over the separated apex and stitched it to the cut vertebral muscles of the scapula—this being done at the same time as the upper stage of a paravertebral thoracoplasty. This complicated and time-consuming technic hardly justifies the advantages gained.

Bull has recently been using Archibald's pectoral graft. Wilms has used free muscle grafts, but found that they became almost entirely transformed into connective tissue, and lost volume; he found, however, that this connective tissue made an excellent bed for a subsequent paraffine graft.

XII. Open Intrapleural Pneumolysis. When adhesions prevent a satisfactory pulmonary compression with artificial pneumothorax, some surgeons open the chest and divide the adhesions with the fingers or with a knife. They claim that this is less dangerous than attempting to stretch or rupture them with high pneumothorax pressure, and that as it is non-deforming, it is preferable to even partial thoracoplasty. If the adhesions are in the upper chest it is usually necessary to resect one rib in order to obtain satisfactory exposure with thoracotomy. Adhesions are divided close to the ribs if sharp dissection is used, thereby attempting to avoid lung tissue or cavities which may be component parts of the bases of some adhesions. Bleeding vessels may be directly ligated or closed with a cautery.

Bertier, Rist and Lecène report a favorable result, that is, a previously insufficient pneumothorax compression was made sufficient. Bertier and Delage report a failure. Schottmüller and Gravesen reports very favorable results from manual separation of the adhesions; Rivière and Romanis a satisfactory separation, but the later development of a thoracic sinus. Eden reports the rupture of a superficial cavity to the pleura several days after operation. Sauerbruch

in 1920 reported 5 cases in which he made a small incision in the chest wall and severed the adhesions with a thermocautery: 1 did well; 1 did well for three months and then the formation of a purulent exudate demanded an extrapleural thoracoplasty which was successful; 1 died in two days; 1 in three weeks, and 1 died after a thoracoplasty which the condition demanded: in the last 2 cases he attempted to separate adhesions from over the entire upper lobe.

The reported results clearly indicate that open intrapleural pneumolysis is a dangerous procedure; the results of partial thoracoplasty or partial extrapleural pneumolysis, or phrenicotomy combined with partial pneumothorax are far superior.

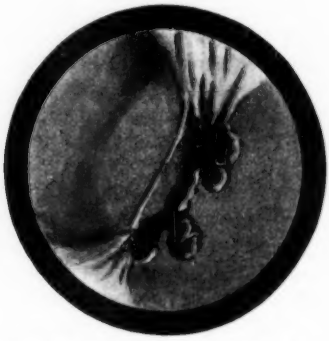

FIG. 10.—Two cord-like adhesions stretching across a partial artificial pneumothorax, as seen through a thoracoscope. The heavier one has been partly burned through with an electrical cautery. (After Unverricht.)

XIII. Closed Intrapleural Pneumolysis. Jacobaeus has devised a method of dividing adhesions without the need of open thoracotomy. He introduces two cannulæ under local anesthesia, near where the roentgen-ray shows adhesions that are preventing sufficient compression with artificial pneumothorax; into one he introduces his "thoracoscope," which is similar to a cystoscope, and which enables him to see the adhesions to be severed; into the other he inserts a thermocautery which burns through the adhesions.* He has completed this operation successfully in 55 (73 per cent) of 75 cases; Gravesen in 22 (63 per cent) of 35 cases; Unverricht completely cauterized 4, and incompletely cauterized 4 of 10 cases; Jacobaeus and five other physicians successfully cauterized 85 (70 per cent) of 121 cases.

This procedure is open to many objections. When completely successful it merely prepares the patient to receive a total artificial pneumothorax. In Jacobaeus' hands there has been a mortality

* The necessary instruments, including a tissue specimen remover, as designed by Unverricht, may be purchased from Georg Wolf, Karlstr. 18, Berlin.

of 6 per cent. He considers conveniently located adhesions up to "little finger size" suitable for cauterization. Holmboe has seen it followed by hemorrhage, pyopneumothorax and thoracic sinus; several times he saw signs of shock. He examines all of his pneumothorax patients with the thoracoscope. Of the 27 in his published series 9 needed the cautery; of these 9 the artificial pneumothorax made possible by the operation was successful in 5, partially successful in 2, and unsuccessful in 2. An attempt of his to burn through a too thick ("thumb-sized") adhesion resulted in virulent empyema and death.

Cauterization is frequently followed by effusion which may become purulent and secondarily infected. A patient of Jessen's died of a purulent exudate and progression of the tuberculosis. Seven of Jacobaeus' 75 cases, 6 of Gravesen's 35, and 5 of Unverricht's 10 were complicated by tuberculous empyema, some of them fatal. Jacobaeus believes it usually possible to distinguish a prolongation of a pulmonary cavity into an adhesion by its bluish color and by the fact that it bulges when the patient coughs, and so to avoid it. Lung tissue or prolongation of a cavity capable, if opened, of infecting the pleura, may extend 1.5 cm. into any adhesion of diameter greater than 1 cm. If bleeding occurs from the severed end of an adhesion usually it may be controlled with low heat in the cautery, or with the special forceps devised for the purpose by Holmboe, or by injecting sufficiently large quantities of normal saline solution into the pleural cavity (Jacobaeus). Among the 200 reported cases of adhesion cauterization, there have been 7 hemorrhages from the severed adhesions, and 1 of these was fatal.

The smoke generated by the cautery may so cloud the field of vision that further cauterization must be postponed, or attempts made to aspirate the smoke-laden air. Sudden movements of the patient may cause the cautery to enter the lung. If it sticks it must be jerked loose, and this is very painful. Only certain narrow, fairly long adhesions are suitable for division by cautery; after the thoracoscope has already been introduced it may be discovered that the adhesions are not suitable for the operation.

Sauerbruch's opinion, concurred in by Moreau and Olbrechts, is that the dangers and uncertainties of the method do not justify its use simply to make possible a more satisfactory artificial pneumothorax; he has never used it, and would always prefer partial thoracoplasty or extrapleural pneumolysis combined with partial pneumothorax. I believe it will prove a valuable addition to artificial pneumothorax therapy if its use is strictly confined to those patients whose restricting adhesions do not number more than two or three, and are at least 3 cm. in length and not more than 0.75 cm. thick, and which can be burned through in one short operative sitting.

Paralysis of Diaphragm. In 1911 Stuertz proposed phrenicotomy for progressive lower lobe tuberculous lesions, especially for

cavity. Since then its indications have been widely extended, and modifications of technic introduced; in Sauerbruch's Clinic alone it has been used several hundred times for many kinds of disease.

The phrenic nerve takes origin from cervical roots III, IV and V. Its main stem runs inferiorly and internally, obliquely across the scalenus anticus muscle and beneath the subclavian vein to the diaphragm. From the inferior cervical sympathetic ganglion and from the suprapleural plexus it receives some sympathetic fibers. Twenty or 30 per cent of all persons have an accessory phrenic, which usually arises from the fifth cervical root and runs together with the nerve to the subclavius, or separately, in front of the subclavian vein to join the main phrenic stem 4 to 5 cm. from the first rib, just centrad to the pulmonary hilus. Very rarely an accessory phrenic may arise from some other root than the fifth cervical, and descend separately or with the ansa hypoglossi. The periphery of the diaphragm also receives sensory nerve fibers from the lower six intercostal nerves; the twelfth nerve supplies motor innervation to the few fibers arising from the twelfth rib, but the other intercostal nerves carry no motor fibers to the diaphragm (Willy Felix).

Complete paralysis of one-half of the diaphragm by interruption of both main and accessory stems of the phrenic causes that half to rise passively into the chest and to remain at rest, except that its central tendon may be tugged at slightly, almost negligibly, by the normal movements of its other half, or that it may move slightly, in a paradoxical sense, with the respiratory changes of pressure of its pleural cavity (Kienbock's phenomenon). The diaphragm atrophies and becomes a parchment-like membrane; unless hindered by many pleural adhesions, or an unusually stiff infiltrated lung, it may be expected to continue to mount into the chest cavity for some months after operation. Clinically a certain amount of pulmonary rest and compression are produced, especially of the lower lobe, and if there are no pleural adhesions the upper lobes are similarly affected. It is more exact to speak of a relaxation of the lung than of a compression. Even when the tuberculous lesions are predominantly in the upper lobes it is usual for some clinical improvement to follow phrenicotomy: fever, pulse, cough and expectoration become less, and upper lobe cavities may be seen by roentgen-ray to be definitely narrowed (Zadek). Contrary to expectation, cough and expectoration are easier after paralysis of the diaphragm than before; this is explained on the grounds that a lax diaphragm allows the strong abdominal muscles, always much relied upon in coughing, to act more quickly. Phrenicotomy has not been known to cause dyspnea or other respiratory disturbance. In fact Jehn, Sauerbruch, Lehman, Dehler and Stern have performed bilateral phrenicotomy for persistent singultus, or to permit artificial respiration in diaphragmatic tetanus, and have seen no noteworthy respiratory disturbance; Jehn's patient led an active life three and a half years after the operation and was never dyspneic.

Observations upon Walter's patients who had had "simple phrenicotomy" (no attempt to resect the accessory branch when present) showed that some of the diaphragms resumed small normal, instead of paradoxical, movements within a month of operation (Goetze has seen this occur within a few days); it may be assumed that their accessory phrenics had compensated. Fritz saw small normal diaphragmatic movements in 25 per cent of simple phrenicotomies. After radical phrenicotomy (which includes resection of the accessory branch) the diaphragm never regains its tone nor loses its slight paradoxical movements; the state of functional rest is nearly absolute.

After a simple phrenicotomy the diaphragm rises to a level 3 to 7 cm. higher than normal, and higher on the right than on the left. Normally the right diaphragm is 1 to 2 cm. higher than the left; on forced inspiration there may be a difference of 2 to 4 cm. Chaoul and Stierlin state that scarcely any change in form is visible by roentgen-ray in the costophrenic sinus after phrenicotomy.

H. Alexander, reporting 14 of Sauerbruch's and Schreiber's cases, found an average rise of 2.15 cm. after simple phrenicotomy and 4.25 cm. after radical phrenicotomy. In 17 cases of simple phrenicotomy Fritz found the difference between the two halves of the diaphragm to be 2 to 4 cm. in full inspiration; in 11 cases of radical phrenicotomy the difference was 7 cm. when the right side had been paralyzed, and 4 cm. when it had been the left side. Willy Felix found the average differences in diaphragmatic height after right and left sided radical operations upon 20 patients to be 7 cm. on inspiration, 3 cm. on expiration. Sultan has seen as great a difference as 11 cm. after right radical phrenicotomy, and 9 cm. after left-sided operation. Sauerbruch gives the differences after radical phrenicotomy as follows: After right-sided operation, right diaphragm 4 cm. higher than left in expiratory position, and 8 cm. in inspiratory position; after left-sided operation, left diaphragm 2 cm. higher than right in expiration and 6 cm. higher in inspiration. Spirometer readings are reduced 30 per cent by the operation.

Ken Kure and his co-workers found that the right diaphragms of apes did not rise after phrenicotomy; their explanation is that the weight of the liver pulling the diaphragm down more than counterbalances the negative pressure in the thorax pulling it up. Shulte-Tigger says this does not occur in man, and Felix specifically states that his fluoroscopical observations of high right-sided diaphragms were made with the patients in the erect posture.

Phrenicotomy has the disadvantages and advantages of all partial operations (see partial procedures under "choice of operation"). The following are opposed to its use as an independent procedure, but advocate it warmly as supplementary for certain cases: Sauerbruch, Brauer, Denk (experience of 26 cases), Zadek (ten years' experience), L. Spengler, Walter, Baer, Shulte-Tigger, Maendl, Felix and Sultan. Only Goetze, Frisch, Fischer and H. Alexander advise it as

an independent operation in certain cases when artificial pneumothorax is not realizable. Goetze says that 50 per cent of the cases are improved and many of them cured. Sauerbruch believes that many so-called "cures" after phrenicotomy used alone are only apparent cures, and that relapses often follow.

In addition to the advantages that may be derived from any partial operation phrenicotomy, in particular, may be valuable as: (1) A test of the better lung when thoracoplasty is being considered (see the better lung under "indications and contraindications"). Sultan advises it as a preliminary to any thoracoplasty; also to help fill empyema cavities. (2) As a preliminary to a complete thoracoplasty when the lower lobe is much diseased, or when the chest is greatly contracted and the heart displaced by the pull of fibroid phthisis or pleural scars. The final total compression and repose of the lung are greater. (3) Preliminary to a partial thoracoplasty of the upper chest in cases where the lower lung is free of disease. Sauerbruch, however, does not consider phrenicotomy without partial resection of the lower ribs sufficient assurance against aspiration at the time of operation on the upper ribs. (4) To cause enough clinical improvement in desperately sick patients to permit a later thoracoplasty; the interval should be two to three months (H. Alexander). (5) In conjunction with incomplete artificial pneumothorax. Shulte-Tigger believes that this combination has a wide and valuable field. He and Frisch consider it especially indicated where there are basal adhesions, as basal lesions are usually grave enough to demand maximum and prolonged rest and compression. (6) For the pain, dyspnea and irritative cough caused by diaphragmatic adhesions in some cases of artificial pneumothorax. (7) As supplementary to every artificial pneumothorax (Baer), in order to lessen the occurrence of exudate, and to lengthen the time intervals between gas "fills," and to decrease the size of the chest against the time when a shrunken, inelastic lung is permitted to expand on release of the pneumothorax (Goetze, Zadek, Sultan and Frisch). Zadek and Sultan have used the combination in over 50 cases since 1922, and so far are hugely pleased with the results. Zadek says that there is less displacement of the mediastinum than when pneumothorax is used alone.

Sauerbruch and Zadek call attention to the newly observed fact that fewer exudates occur in cases of artificial pneumothorax when the diaphragm has been paralyzed, and that when they do occur they are smaller. Intrapleural gas is absorbed so slowly after diaphragmatic paralysis that some patients who needed "refills" every three to four weeks before phrenicotomy, need them only every ten to twelve weeks after phrenicotomy (Sauerbruch); Zadek says that phrenicotomy lengthens the intervals between "fills" from a quarter to a third; Goetze and Frisch have advised diaphragmatic paralysis when expansion of the lower lobe by the tug of new adhesions under an effusion is feared.

To release an artificial pneumothorax and permit a scarred, shrunken lung to expand in an attempt to meet the chest wall is a hazardous procedure and not rarely followed by emphysema, mediastinal displacement, dyspnea, effusion, pain, unfolding of cavities, lighting up of infirmly encapsulated foci, and reactivation of the tuberculous disease. The narrowing of the chest, caused by the mounting of the diaphragm, largely compensates for the disproportion in volume between the unchanged capacity of the hemithorax and the diminished volume of the shrunken, fibrotic lung. I believe that these many advantages will eventually lead to the use of phrenicotomy in conjunction with almost every case of artificial pneumo-

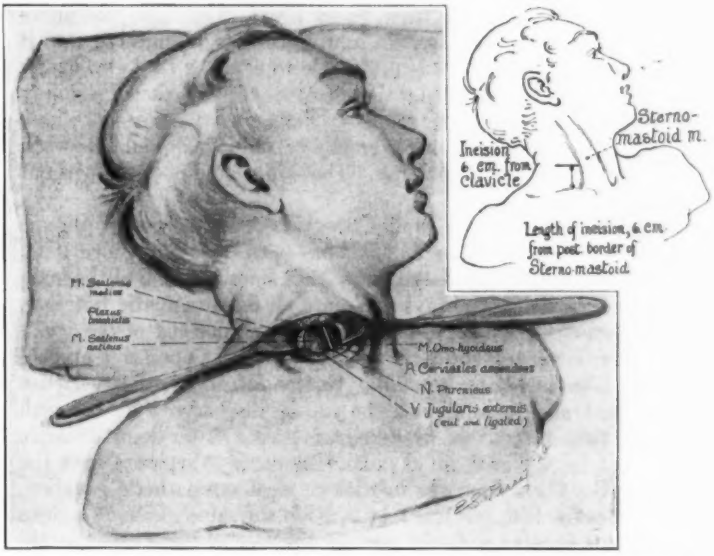
Sterno-mastoid m.
Incision 6 cm. from clavicle
Length of incision, 6 cm. from post. border of Sterno-mastoid
M. Omo-hyoideus
A. Cervicalis ascendens
N. Phrenicus
V. Jugularis externa (cut and ligated)

FIG. 11.—Author's incision for phrenicotomy. Surgical anatomy of the approach to the nerve.

thorax. Zadek now performs it eight to fourteen days prior to the induction of artificial pneumothorax treatment; he believes that the negative pressure within the pleura causes the diaphragm to mount higher than if paralysis did not occur until the pleural pressure were positive. Maendl finds that the positive intrapleural pressures of pneumothorax (in one case: +1, +3 cm. H_2O) do not depress the elevated, paralyzed diaphragm. Goetze performs phrenicotomy after the pneumothorax. As diaphragmatic adhesions form quite rapidly after phrenicotomy it is unwise to wait over three weeks before starting the pneumothorax. For patients with history of hemoptysis Zadek does not perform phrenicotomy until after the pneumothorax treatment has been started.

Simple phrenicotomy is strictly a minor operation. It is performed under local anesthesia in a few minutes. Commencing at the posterior border of the sternomastoid muscle 6 cm. above the clavicle, a 6 cm. transverse incision is made in the posterior triangle of the neck. The Continental surgeons use a longer incision along the posterior border of the sternomastoid muscle; it is unnecessarily disfiguring. The transverse incision leaves almost no noticeable scar. In the fatty tissue between the skin and scalenus anticus muscle some veins and branches of the transverse cervical and suprascapular arteries may require ligation. Running across the anterior surface of the muscle, obliquely from above down and in, is the phrenic stem. Galvanic stimulation or pinching of it causes singultus and pain in the shoulder, neck, chest, heart, diaphragm and abdomen. A few drops of novocain solution should be injected into it before it is sectioned. It is preferable to resect 2 to 4 cm. of the nerve, as Kroh has found that there may be regeneration of a simply sectioned nerve within four months. Felix cites two patients whose diaphragms were functioning normally one and a half and five years, respectively, after phrenicotomy. The skin wound is closed without drainage.

Radical phrenicotomy implies resection of the accessory phrenic as well as of the main stem. This has been done only since 1921. As long ago as 1884 De Jaeger knew that simple section of the main phrenic stem did not always eliminate all diaphragmatic function. Recently Felix and Goetze have studied the anatomy of the accessory phrenic nerves, and have proposed different operative procedures to interrupt their function. Goetze considers other varieties than the branch arising with the subclavius nerve from the fifth cervical root so rare that he disregards them. After doing a simple phrenicotomy as far down as possible in order to separate from the phrenic the fibers from the inferior cervical sympathetic ganglion, he exposes the fifth cervical root through the same incision (he uses a long one parallel with the posterior border of the sternomastoid muscle), and identifies the desired branch on its (C-V root) anterior surface, and sections it. Felix performs a Thiersch exæresis of the phrenic nerve, twisting it out of the chest from beyond the place where accessory phrenics usually join it (7 cm. from the first rib, or 12 cm. from the place where the phrenic is conveniently sectioned on the scalenus anticus muscle. After giving a hypodermic of morphin. Felix employs the same incision as for simple phrenicotomy, and operates under local anesthesia; he injects 20 cc novocain solution around cervical nerve roots III to V in order to block centripetal pain impulses from the accessory phrenic. He then identifies the main phrenic stem on the scalenus anticus muscle, sections it and seizes the distal cut end with a Thiersch or hemostatic forceps, whose jaws are protected, and slowly twists the nerve until it breaks. The nerve should be carefully freed of connective tissue before it is seized, and the twists should not be faster than one in one minute.

(*To be continued*)

REVIEWS.

HYGIENE AND PUBLIC HEALTH. By GEORGE M. PRICE, M.D., Director of Joint Board of Sanitary Control and Director of Union Health Center, New York City. Third edition. Pp. 306. Philadelphia and New York: Lea & Febiger, 1924.

THE book is an epitome of the subject, presenting only the most salient features, and even these of necessity quite briefly. As the author says "Some subjects upon which volumes have been written are disposed of in a few lines." Considering the scope of the work, however, this has been well done. To the new third edition have been added chapters on hygiene of childhood and on food, that add considerably to the value of the work. K.

A TEXT-BOOK OF PHARMACOLOGY AND THERAPEUTICS OR THE ACTION OF DRUGS IN HEALTH AND DISEASE. By ARTHUR R. CUSHNY, M.A., M.D., LL.D., F.R.S., Professor of Materia Medica and Pharmacology in the University of Edinburgh. Eighth edition. Pp. 707; 73 illustrations. Philadelphia and New York: Lea & Febiger, 1924.

IT is a pleasure to note that after a period of twenty-one years this excellent monograph has been revised and brought up to date. The chief changes are to be found in connection with cardiac therapeutics and the pharmacology of ergot, cocain, thyroid, strychnin and pituitary. A short chapter has been allotted to insulin, another to the vitamins and one to histamin action and anaphylaxis. The work as it stands will hardly find a rival in the English language as a text-book on pharmacology. A.

THE INTERNATIONAL MEDICAL ANNUAL, A YEAR BOOK OF TREATMENT AND PRACTITIONER'S INDEX. Pp. 556; 54 plates, 99 illustrations. New York: William Wood & Co., 1924.

THIS annual publication is a compendium by recognized authorities in which the recent advances in medicine and surgery are

outlined. The alphabetical arrangement according to disease is a feature of distinct advantage for ready reference. Noteworthy discussions in this issue relate to desseminated sclerosis, diabetes, asthma and the functional neuroses, by Purves-Stewart, Comrie, Wynn and Hadfield respectively A.

DISEASES OF THE CHEST AND THE PRINCIPLES OF PHYSICAL DIAGNOSIS. By GEORGE W. NORRIS, M.D., Professor of Clinical Medicine in the University of Pennsylvania, and HENRY R. M. LANDIS, M.D., Director of the Clinical and Sociological Departments of the Henry Phipps Institute of the University of Pennsylvania, with a chapter on the Electrocardiograph in Heart Disease by EDWARD B. KRUMBHAAR, PH.D., M.D., Director of Laboratories of the Philadelphia General Hospital. Third edition. Pp. 907; 433 illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

THE fact that this book since its first appearance in 1917 has been five times reprinted, including two revisions, is an ample testimony to the continued popularity of this excellent work. By its thoroughness, lucid style and pleasing make-up it has endeared itself to practitioner, teacher and student. The present third edition has been thoroughly revised and certain portions rewritten Some of the rarer cardiac and pulmonary conditions that were omitted in previous editions are taken up, somewhat briefly to be sure, but adequate references are furnished should the reader desire to further search the literature. K.

QUAIN'S ELEMENTS OF ANATOMY. MYOLOGY. By T. H. BRYCE, M.D., F.R.S., Professor of Anatomy in the University of Glasgow, with sections on the actions of muscles by THOMAS WALMSLEY; Professor of Anatomy, Queen's University of Belfast. Vol. IV. Eleventh edition. Pp. 310; 91 illustrations, of which 53 are colored plates. New York and London: Longmans, Green & Co., 1923.

THIS is the most recent volume in the eleventh edition of Quain, and it is interesting that its author, Professor Bryce, was also the author of the first volume of this edition, which was devoted to Embryology, and appeared in 1908. The part preceding the present was published in 1915, and the long interval which has elapsed between the two parts has been due to circumstances arising from the war. But this delay has in no way impaired the

quality of the final result. The subject is treated from a dynamic standpoint, as is proper for such a plastic system, in which so many considerations of development, phylogeny and function enter into the final product. Here is given not merely a catalogue of morphological entities, but also a functional study, which approach in places a real physiology of the muscular and fascial systems. The embryological knowledge of the author is shown in references to the development of various groups of muscles from premuscle tissue and muscle masses in young embryos, and their nerve connections. Seventeen pages of bibliography, mostly of the last twenty-five years, show that the scientific study of the subject is far from being a finished one. The colored plates of the various dissections will appeal to the student, while the detailed accounts of the fascia, bursæ and tendon sheaths will be referred to by the surgeon and physician. A.

STUDIES ON SCHISTOSOMIASIS JAPONICA. By ERNEST CARROLL FAUST, PH.D., and HENRY EDMUND MELENEY, M.D., with a supplement on the molluscan hosts of the human blood fluke in China and Japan, and species liable to be confused with them, By NELSON ANNANDALE, D.SC. *The American Journal of Hygiene*, Monograph Series No. 3, March, 1924.

THIS monograph of 339 pages is the coöperative undertaking of the Associate Professor of Parasitology and the Associate in Medicine in the Peking Union Medical College, Peking, China, and the Director of the Zoölogical Survey of India, Calcutta, India. The authors discuss the historical aspects of schistosomiasis, the morphology, biology and life history of the causative organism, its mode of migration in the body of the mammalian host, the intermediate hosts, the distribution of schistosomiasis in the Orient; the pathological anatomy, clinical manifestations and prophylactic aspects of the disease and, finally, the molluscan hosts of the human blood fluke, and the species liable to be confused with them. The work is well printed and illustrated with 36 plates and 25 test figures. The bibliography given is very complete. This excellent monograph is warmly recommended to those interested in tropical or parasitic diseases. S.

DISLOCATIONS AND JOINT FRACTURES. By FREDERIC T. COTTON, A.M., M.D., Visiting Surgeon to the Boston City Hospital; Associate in Surgery, Harvard Medical School. Second edition. Pp. 740; 1393 illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

THE reader needs no introduction to the author, nor to this the second edition of his work, for all who read on this subject must

needs have met them both at least in print. It is needless to say the book is good. The author has covered his subject most carefully and thoroughly, and in doing so has brought his own personal cases and illustrations to help elucidate the matter. He is responsible entirely for the text and for all the drawings, so that the question or the possibility of mistakes due to misinterpretation is reduced to a minimum. The book fills the wants of not only the general practitioner, but also of those who specialize in the treatment of bones and joints. It is thorough, comprehensive, lucid, nicely written, profusely illustrated and instructive. E.

OPERATIVE SURGERY. Covering the Operative Technic Involved in the Operations of General and Special Surgery. By WARREN STONE BICKHAM, M.D., F.A.C.S., former Surgeon-in-Charge of General Surgery, Manhattan State Hospital, New York, and former Visiting Surgeon to Charity and to Touro Hospitals, New Orleans. In six octavo volumes. Volume III. Pp. 1001; 1249 illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

VOLUME III deals with operations upon the head, neck and thoracic wall. The special fields of the eye, ear, nose and throat are covered in a manner satisfactory for general purposes. Plastic surgery is well covered in sections upon the cheeks, lips and palate. Most surgeons, however, will not agree that it is best to wait until after the second year to repair a cleft palate. The chapter on the thyroid gland is not up to standard and a sense of proportion is violated in allotting but thirty-five pages to this subject when thirty-six pages are given to the esophagus. Throughout the book it is felt that its value would be greater if more space were given to operations of choice and less to those of occasional use or historical value. P.

OPERATIVE SURGERY. Covering the Operative Technic Involved in the Operations of General and Special Surgery. By WARREN STONE BICKHAM, M.D., F.A.C.S., former Surgeon in Charge of General Surgery, Manhattan State Hospital, New York, and former Visiting Surgeon to Charity and to Touro Hospitals, New Orleans. In six octavo volumes. Vol. IV. Pp. 842; 6378 illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

VOLUME IV deals with the heart, pericardium and intrathoracic vessels, the thoracic portion of the esophagus and other intrathoracic

structures, the abdominal wall and hernia, the peritoneum and abdominal viscera. Discussion is fuller and more illuminating than in the preceding volume. The arrangement, illustration and typography are excellent as in the preceding issues and as a reference book it is unsurpassed. The reviewer does not wish to detract from these obvious merits unduly, but considering the influence which such a pretentious work will have on surgical practice in smaller clinics throughout the country he could wish that display and illustration might go hand in hand with utility. For instance, the space and illustrations given to Loreta's and Hahn's obsolete operations of pylorodiosis could have been curtailed in favor of a fuller description of Rammstedt's operation. Polya's method and Balfour's modification of gastric resection are certainly more useful than Kocher's, but receive less attention and no credit. Fig. 3529, which purports to show how to avoid vicious circle in gastroenterostomy by depicting the isoperistaltic manner of placing the jejunal loop as the proper method and the non-isoperistaltic method as dangerous, overlooks the fact that the latter is the operation employed by the Mayo Clinic and, under their influence, by the greater number of surgeons in this country, and has nothing to do with vicious circle. In spite of these comments which are offered as suggestions rather than strictures the book is commended as a valuable addition to the surgeon's library. P.

PATHOLOGICAL TECHNIC. A Practical Manual for Workers in Pathological Histology and Bacteriology, Including Directions for the Performance of Autopsies and for Clinical Diagnosis by Laboratory Methods. By FRANK B. MALLORY, M.D., Pathologist to the Boston City Hospital; and JAMES B. WRIGHT, M.D., Pathologist to the Massachusetts General Hospital and Assistant Professor of Pathology, Harvard Medical School. Eighth edition, revised and enlarged. Pp. 180; numerous illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

A NEW edition of this well-known work, the best of its kind in the English language, is always welcomed by pathologists. In the present case it is doubly welcome after a lapse of six years, since the previous edition, instead of the usual three years. More than one hundred pages have been added, chiefly in the chapters on histology, on the nervous system (by S. T. Orton) and on the blood, the last (contributed by Dr. Buckman) now including sections on hemoglobin, coagulation, volume, resistance, reticulocytes and so forth. There is a small section on medical photography, which if it helps in obtaining results in any way comparable to those of Dr. Mallory will be indeed welcome. The omission of the small section

on methods of examination of tissues and fluids is to be regretted, but this is more than compensated for by the valuable new inclusions. K.

RADIUM REPORT OF THE MEMORIAL HOSPITAL, NEW YORK. Second series, 1923. Pp. 305; 55 illustrations. New York: Paul Hoeber, 1924.

THIS report consists of articles by the various members of the staff of the Memorial Hospital. In the seven years intervening between the publication of the first report and this one the radium therapy of malignant tumors has made great strides forward, and in this advance the Memorial Hospital has been the pacemaker in this country. For this reason their careful conservative conclusions on selection of cases, the technic of therapy and the results of treatment can be accepted as the best available in the field. The book is primarily of interest to radium therapists, yet the internist can form from it opinions based on the widest of clinical experience as to what tumors are best suitable for radium therapy, and what results are to be expected. L.

THEORIES OF MEMORY. By BEATRICE EDGELL, M.A., PH.D., University Reader in Psychology, Medford College, University of London. Pp. 174. New York: American Branch, Oxford University Press, 1924.

THE author reviews some of the theories of memory that have been advanced in the past, in particular the biological doctrine of behaviorism and the memory conceptions advanced by Bergson, Russell, Alexander and Holt. Criticisms and objections are raised, and an attempt to answer them made in a discussion of memory as a purely psychological conception. The work is of interest to physiologists and psychologists alike, but because of its highly technical character has only a limited appeal. K.

THE CULTURE OF THE ABDOMEN. By F. A. HORNIBROOK. Pp. 67; 26 illustrations. New York: William Wood & Co., 1924.

THIS is a very excellent book by an author who seems to have had a large amount of experience in the treatment of the disorder he wishes to remedy. Like most faddists, he attributes entirely too much to obesity and chronic constipation, but, as with most enthusiasts, he probably feels that this is necessary in order to impress the

reader with the validity of his contention. There is no doubt that a great deal of what he has to say is true and, what is more important, that excellent results are shown by the methods of treatment which he details for the strengthening of the abdominal muscles and improving intestinal peristalsis. M.

COLLECTED PAPERS OF THE MAYO CLINIC AND THE MAYO FOUNDATION. Pp. 1377; 410 illustrations. Philadelphia: W. B. SAUNDERS Company, 1924.

THE fifteenth volume of the collected papers of the Mayo Clinic and the Mayo Foundation presents a decided change over the previous volume. The reviewer in the past has pointed out that the inclusion of so many papers as appeared in previous volumes has made a tome which had become unwieldy and too large for practical purposes. The editors of the new volume have also concluded that such is the case, so the present volume, although it represents a collection of every paper that is published during the year from the Mayo Clinic and the Mayo Foundation, has been reduced about half in the number of pages of contents by careful editorial supervision and by abstracting the articles that are largely technical or of interest limited to specialists. The reviewer feels that this is a decided improvement. The contents of the volume are most catholic in their quality. There are articles on almost every type of disease and disease of practically every organ in the body as well as a large number of articles more or less of a general character. M.

THE RELATIVE POSITION OF REST OF THE EYES AND THE PROLONGED OCCLUSION TEST. By F. W. MARLOW, Professor of Ophthalmology, Syracuse University. Pp. 94; 27 tables and charts. Philadelphia: F. A. Davis Company, 1924.

IN this essay the author discusses the inadequacy of the ordinary muscle balance tests in determining the absolute amount of heterophoria, and describes the technic and value of the prolonged occlusion test for bringing out the full muscle error. In applying this test he uses a ground-glass, a piece of black paper pasted on the back of one glass, or, better, a patch over one eye. The faulty eye is always occluded, and the average duration of occlusion is seven days.

By this method the author elicits the latent heterophoria, which may not have been apparent or only to a slight degree with the rapid test. Exophoria and left hypophoria are present in the

majority of cases. Heterophoria by this test has no relation to age, but may run in families. The only practical objection to the use of the prolonged occlusion test in routine practice is the number of days required to complete it. S.

PALEOPATHOLOGY: AN INTRODUCTION TO THE STUDY OF ANCIENT EVIDENCES OF DISEASE. By ROY L. MOODIE, Associate Professor of Anatomy in the University of Illinois. Pp. 567; 49 figures and 117 plates. Urbana, Ill.: University of Illinois Press, 1923.

THIS comprehensive and scholarly volume is a prominent milestone in this most recent branch of the science of pathology. The book is dedicated to Sir Marc Armand Ruffer, who recoined the term Paleopathology, and whose work "on the pathology of ancient mummies forms the groundwork" of the science today. Ruffer's collected studies, published by the University of Chicago Press in 1921, under Moodie's editorship, is the first book of consequence on this subject in English. The second, the book now under view, extends the ground to be covered from the Proterozoic period, 100,000,000 or more years ago, to the beginning of the historical period. Most of the evidence naturally comes from fossil invertebrates and reptiles and other early vertebrates and is necessarily confined almost entirely to shell or bony lesions. Such compelling subjects, therefore, as the causes of extinction of races, have still to be left to conjecture: The bony lesions observed are for the most part compatible with life and many probable causes would obviously have left no trace. Such speculations are legitimately indulged in by the author (Cp. "The possibility of a widespread epidemic of the *nagana* among the ungulates of the early Tertiary, a million or more years ago"), in a manner calculated to hold the interest of the reader and stimulate further studies, without building ladders of sand. The last four chapters on the pathology of the early human races (Stone ages, Egyptians, Pre-Columbian Indians and Peruvians) will perhaps especially interest the average medical man. Prehistoric trephining with stone implements (still continued by the North African Kabyles, in Tahiti, Bolivia and elsewhere) and other primitive surgical methods have received considerable attention; but it will probably be an interesting surprise to most readers to learn that appendicitis, arteriosclerosis, hydrocephalus, poliomyelitis, prolapsus recti, psoas abscess, rickets and many other disorders have been observed in corpses from four to ten thousand years old. K.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE MEDICAL SCHOOL AND ASSOCIATE PROFESSOR OF SURGERY IN THE SCHOOL FOR GRADUATES IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

Eventration of the Diaphragm.—WALTON (*Am. Jour. Roentgenol.*, 1924, **2**, 420) says that the term eventration represents a condition in which one dome of the diaphragm is stretched out and elevated high into the thoracic cavity, so that the abdominal viscera immediately beneath are contained within the thorax. In diaphragmatic hernia the abdominal viscera are displaced into the thoracic cavity through a normal or pathological orifice in the diaphragm. Eventration does not necessarily produce symptoms. When these do occur they are usually referred to the cardiopulmonary or digestive organs. It is found four times more frequently in men than in women. The theory of congenital origin is substantiated by the fact that it has been found in a number of infants and is usually associated with other congenital defects. It nearly always involves the left side of the diaphragm, the top of the dome, often reaching as high as the second or third interspace, anteriorly. The viscera in ectopia are usually the stomach, colon, small intestines, liver, spleen and kidney. Only 6 cases of eventration of the right side have been reported. Case reports and roentgen-ray pictures are appended to the article.

Goiter.—MCCARRISON (*Brit. Med. Jour.*, 1924, **1**, 989) states that there are two main factors on which the prevention and cure of goiter depend, namely: The general hygiene of the individual, especially of the intestinal tract, and the amount of iodine available for the needs of the thyroid gland and the organism generally. It is not always necessary that the water supply should be bacteriologically impure in order that the bacterial conditions in the intestines favorable to the production of goiter shall be set up. Constipation and imperfect drainage of the bowel may be equally effective in producing them, with

the hygiene at high mark; the method of prevention of goiter by iodine is at once simple, rational and cheap, and no ill consequences have been observed when it is applied in the proper way and at the proper time.

Further Observations of the Kahn Reaction in the Serological Diagnosis of Syphilis.—KEIM (*Am. Jour. Syphilis*, 1924, **8**, 323) reports that preliminary studies showed that the clinical application of the test compares favorably in sensitiveness with the standard Wassermann reaction. The advantage of this precipitation test over the complement-fixation test are simplicity of procedure, rapidly of reading, reduction of sources of error, through the elimination of the hemolytic system. The clinical application of the Kahn test has been studied in 1000 cases. Two-thirds of this series were carried out by Kahn's latest procedure, in which three different serum-antigen proportions are employed and the tests are completed a few minutes after mixing serum with antigen. The results obtained indicate that the newer procedure possesses a higher degree of sensitiveness.

Clinical Observations on the Etiology of Gall Stones in Women.—SCHROYER (*Surg., Gynec. and Obst.*, 1924, **38**, 344) says that cholecystitis of middle adult life in women in a large number of cases traces its origin to the first pregnancy, and as such it must be recognized as a distinct clinical entity. If this conclusion is supported by observations of other clinicians it may tend to destroy the clinical superstition that young women do not have gall stones. It may train medical men to link vague abdominal phenomena occurring during the first pregnancy and recurring during the subsequent pregnancies with the clinical finality of the gall-stone picture present in patients between the ages of thirty-five and forty-five years.

Operative Treatment of Congenital Dislocation.—DICKSON (*Jour. Bone and Joint Surg.*, 1924, **6**, 262) states that absolute failure occurred in 1 of 5 cases. This failure was due to infection and not the operation. Admitting that infection is probably a certain cause of failure, it does not seem that the possibility of its occurrence is a contraindication to operative interference in these cases. The benefit which the 4 successful cases secured was due more to stabilizing the hip-joint than to the increase in length secured. The only limitation of motion which has occurred has been inability to acutely flex the hip, and this is comparatively unimportant, as it is a movement which is only occasionally used.

The Etiology and Treatment of Non-tuberculous Pulmonary Abscess.—WHITTEMORE (*Surg., Gynec. and Obst.*, 1924, **38**, 461) says that it is important for the surgeon performing the operations on the upper respiratory tract under general anesthesia to bear in mind the danger of lung infections and arrange his technic so as to avoid this complication. From 10 to 30 per cent of the cases may be expected to be cured by expectant treatment. Artificial pneumothorax may cure a very small number of cases. It should be used only in those cases in which the lung and costal pleura are not adherent. It is an excellent means of determining whether or not adhesions are present. Bronchoscopy

may cure a very limited number of cases if treatment is established early. Surgery offers an excellent chance for cure in those cases in which other methods of treatment have failed or are unsuitable.

Epididymotomy for Acute Epididymitis as an Office Procedure.—DORSEY (*Am. Jour. Surg.*, 1924, **38**, 4) says that epididymitis is practically always secondary to inflammation of the deep urethra in the region of the ejaculating ducts. The urethral inflammation is usually associated with involvement of the seminal vesicles and prostate gland. The severity of the epididymal inflammation bears no relationship to the degree of involvement in the deep urethra. Epididymotomy invariably affords immediate and permanent relief from pain. There are no recurrences after operation, unless there is a fresh infection. The course of epididymitis is without question shortened, as is also the urethritis. Patients are probably less likely to be sterile. Treatment of the urethritis can be begun much earlier. Finally the operation can be safely and successfully performed in the office under local anesthesia.

Testicular Grafts.—WALKER (*Lancet*, 1924, **206**, 319) reports that the results obtained from the treatment of testicular deficiency by means of grafts are distinctly promising. The method, however, has its limitations, for in very few of the cases that present themselves for treatment with signs of testicular deficiency is the deficiency entirely confined to the testicle. A question of greatest importance is that of the durability of grafts. The author and other authorities believe that a heterograft undergoes processes of absorption from the very beginning. Morris made the interesting observation that in 1 of his cases possessing testicles, although atrophied ones, the insertion of a graft stimulated the growth of the patient's own testes. A somewhat similar action may possibly be exerted on other endocrine tissue and the impetus given by the graft thus outlasts its life.

Dependent Drainage of the Perivesical Region.—CHUTE (*Jour. Urol.*, 1924, **11**, 365) describes a simple method of dependent drainage with appended case reports. Such drainage is especially indicated in suppurations that involve the loose perivesical tissue. The most typical of these conditions is suppurative pericystitis. This type of drainage, may, however, be used to advantage in various operations that involve the probable infection of the perivesical tissues deep in the pelvis near the base of the bladder. Dependent drainage carried out in this manner is much more efficient than any type of uphill drainage that we can devise. This drainage is easily carried out. The tissues involved are not important. The time consumed is very short.

The Etiology and Treatment of Non-tuberculous Pulmonary Abscess.—WHITTEMORE (*Surg. Gynec. and Obst.*, 1924, **37**, 461) says that the etiology in his own last 100 cases could be established definitely in all but 8 cases. In 66 cases there had been an operation on the upper respiratory tract under general anesthesia directly preceding the lung infection. In 48 cases tonsils had been removed, in 12 patients teeth extracted, in 2 cases septic sinuses drained, in 1 adenoids removed, in 1 a deviated septum straightened, in 1 a broken nose operated upon and

in 1 a tracheotomy was done. Pneumonia was the cause of the abscess in 22 cases. Bronchopneumonia occurred 20 times. Septic infarction was the etiological factor in 3 instances, and a bronchial esophageal fistula in 1. It is important for the surgeon performing operations in the upper respiratory tract, under general anesthesia to bear in mind the danger of lung infection, and arrange his technic so as to avoid this complication. From 10 to 30 per cent of the cases may be expected to be cured by expectant treatment. Artificial pneumothorax may cure a very small number of cases. It should be used only in those cases in which the lung and costal pleura are not adherent. It is an excellent means of determining whether or not adhesions are present. Bronchoscopy may cure a very limited number of cases if treatment is established early. Surgery offers an excellent chance for cure in those cases in which other methods of treatment have failed or are unsuitable.

THERAPEUTICS

UNDER THE CHARGE OF

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NEW YORK.

The Antiallergic Treatment of Bronchial Asthma.—Recognizing the importance of specific agents which, either by ingestion or inhalation, may cause bronchial asthma and emphasizing the necessity of testing all patients who have this condition, by means of skin tests, VAN LEEUWEN (*Therap. d. Gegenw.*, 1924, **3**, 97) states, from the study of 300 cases of bronchial asthma in Holland, that from 80 to 90 per cent of the cases were sensitive to some "miasma" which was peculiar to the climate in which they lived. Two of these "miasma" which are known are found in grain infected with a mite and in grain infected with a fungus, and animal experiments have shown that it is neither the mite nor the mold but some toxic substance which gives rise to the asthmatic attacks. Patients who show specific allergy to food substances should be desensitized only by mouth by giving daily increasing amounts of the food, but never enough to precipitate an attack. Occasionally a patient must be desensitized more than once. Temporary desensitization may be accomplished by giving a small amount of the substance by mouth three-quarters of an hour before meals. If the sensitizing substance is causing attacks by inhalation and cannot be avoided then desensitization may be attempted by injection of the substance in increasing amounts. However, as the great majority of cases do not show any specific allergy, but are sensitive to some agent peculiar to the climate in which they live, bronchial asthma is therefore a climatic disease, and can be successfully treated by changing the patients' residence. This does not necessarily mean residence at a high altitude, although patients are often greatly relieved by residence

in a high altitude, and can there be treated by non-specific antiallergic therapy. The author has used tuberculin for three years for the non-specific treatment of asthma, and finds it gives the most satisfactory results of the various substances tried. Almost all cases of asthma are sensitive to tuberculin and have a general reaction. Among 300 cases only 3 positive cases of tuberculosis were found. The dosage is difficult to determine. He begins with small amounts, gradually increasing until the patient is either free from complaints or a marked local reaction results or the treatment does not help. As soon as the patient is free from complaints injections are given once a week, later once in two weeks without increasing the amount or slightly increasing it. If a local reaction results and the patient feels better then each week a dose is given large enough to give a local reaction. If the patient feels worse then smaller doses are given. If large doses have been given without any results then a new series of injections is given, beginning with very small doses (1 to 100,000,000), and if this series gives no results then tuberculin therapy is useless. If the patient reacts strongly to tuberculin, or if tuberculosis is suspected, then the first dose given is 1 to 10,000,000. In other cases one can begin with 1 to 1,000,000. Old tuberculin (T. O. A. Koch) only is used. At first two injections a week are given subcutaneously, then one a week, and if the conditions are satisfactory one every two weeks and later one every three weeks. In favorable cases, after three or four months, only one injection in three weeks is given, and this is continued for one year. The tendency is to give too large doses, and small doses give the best results. In the first series of 200 cases 50 per cent were cured or almost cured; 38 per cent were improved; 12 per cent were uninfluenced. In the second series of 100 cases, which represented cases already treated with tuberculin by other doctors unsuccessfully, 60 per cent were cured or nearly cured, 25 per cent improved and 15 per cent unimproved. Cases which show return of symptoms after a year's treatment receive a second shorter series of injections. Cases in which climate plays an important role should be kept in their usual environment as much as possible. As tuberculin often gives results only after several weeks, quicker results may be obtained by injections of milk or sulphur in oil. The first milk injection is 0.1 cc subcutaneously; one hour later, 0.5 cc; the next day, 1 cc; then 5 or 10 cc intramuscularly. If the asthma is improved then the milk injections are continued, increasing the amounts 0.5 cc or 0.2 cc. This is continued for one week. After an interval anaphylaxis must be kept in mind, and only 0.1 cc given as the test injection. If there is no change during the fever period then milk therapy is of no use. Sulphur is given with the same object as milk, using a 1 per cent solution of precipitated sulphur in olive oil; 1 cc of a 1 per cent solution of sulphur injected intramuscularly will give a local and general reaction at the end of twelve hours, often with improvement of the asthma. The dose should be selected which will give relief of symptoms and not cause a too severe local reaction; 0.1 to 0.5 cc is often sufficient. Peptone has not given as satisfactory results as has tuberculin, and he considers intravenous injections dangerous in cases showing allergy. Vaccines and autovaccine therapy in asthma, he believes, is founded on wrong theories, as 85 to 90 per cent of his cases showed variation of symptoms with change of climate or stay in the hospital. He believes

that vaccines, particularly stock vaccines, may cause an improvement in the asthmatic symptoms just as is true of several diseases, and in his experience vaccines may cause an increase in the symptoms, while tuberculin gives better results. Patients are put on a purin-free diet because it has been shown that most of these cases have disturbed purin metabolism. Butter, milk and cheese are also prohibited. Carbohydrates are also restricted, and for a long time meat, fish, vegetables and eggs are the basis of the diet. Some cases of asthma have attacks six to eight hours after meals, and are free from attacks when fasting. To these cases rice, zwiebach and tea only are given, with gradual addition of other foods, until a diet is built up. Peptone by mouth is often given as a form of non-specific therapy. Three-quarters of an hour before meals 0.5 gm. of peptone is given and between meals nothing is eaten. This may be tried for a week and continued for one month if there is improvement. Adrenalin, in doses of 0.2 to 0.6 cc is the best substance to counteract symptoms of allergy when they are acute.

An Efficient Intestinal Antiseptic: The Perchlorides of Mercury and Iron in Combination.—Wilson (*Brit. Med. Jour.*, February, 1924, **1**, 270) advocates the use of the perchlorides of mercury and iron as an intestinal antiseptic, and has used this remedy since 1894, when it was first brought to his attention by Wedgewood (*Brit. Med. Jour.*, May, 1894). In cases of enteric fever, colitis and dysentery he has used it extensively, with good results, and gave 15 minims of liquor hydrargyri perchloride and 15 minims of tinctura ferri perchloridi combined with glycerin and chloroform water three to four times a day. As albumins and alkalies destroy the antiseptic action of the perchloride of mercury, the drugs should be given before meals. Some cases have been known to take this mixture continuously for six months without injurious effects. In women it is advisable to omit the dose for a day or two before the menstrual period.

PEDIATRICS

UNDER THE CHARGE OF

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Use of Sulpharsphenamin in Vincent's Angina and Stomatitis in Children.—Barenberg (*Jour. Am. Med. Assn.*, 1924, **83**, 25) and his collaborator Bloomberg used this remedy in cases of Vincent's angina. They point out that there are some cases of stomatitis which are due to lack of antiscorbutic vitamin, and as cases of stomatitis and Vincent's angina have been reported as cured by giving adequate amounts of antiscorbutic vitamin, this protection should be definitely given all cases. In their series the authors gave adequate amounts of antiscorbutic vitamin. They feel that when the condition clears up with this

method that the Vincent's angina has been spontaneously cured as has been noted from time to time in cases of Vincent's angina. The first sign of cure is the subsidence of the adenitis, this swelling disappearing before the lesion itself. Under simple local treatment the glands remain enlarged after the ulceration is healed. It is important to remember that marked improvement in Vincent's angina and ulceromembranous gingivitis treated with intramuscular injections of sulpharphenamin is not apparent until the third or fourth day after injection. It has been shown that sulpharsphenamin exhibits its greatest parasiticidal effect three or four days after injection. The result in Vincent's angina are more remarkable than in gingivitis, because the former is usually more amenable to treatment. This treatment does not rid the mouth of fusospirillar organisms, which the authors found in smears from the gums and tonsils of many children with apparently healthy mouths. The found that sulpharsphenamin is a specific for fusospirillar infections of the mouth and throat, and that one or two injections usually cure. Intramuscular injections combined with local application of sulpharsphenamin hastens this result. In their experience no local or general reactions were encountered in fifty-one injections. This mode of therapy is particularly suitable, as intravenous injection is difficult in children. It is also of value in the treatment of pyorrhea.

The Effect of Tonsillectomy on the General Health of Twelve Hundred Children.—KAISER (*Jour. Am. Med. Assn.*, 1924, **83**, 33) reviewed the data of twelve hundred tonsillectomies, and he feels that there is a great deal of value in the procedure, but that we must not be unmindful of the dangers of the surgical procedure, as well as of the complications that do occur. There is an impressive absence of spectacular results when the observations are controlled by observations on a group not operated upon. The desirability and justification of the operation depends on the ultimate effect on the child. Many years must elapse before the ultimate effect can be determined, but after a period of three years a group of twelve hundred children operated on were compared with an equal number of children not operated upon, and he observed that tonsillectomy offers a child considerable relief from such common complaints as sore throats, head colds and mouth breathing. It lessens the chances of having discharging ears and their complications. It assures some protection against glandular infection, but is no guarantee against it, and it does not assure the immediate disappearance of enlarged cervical glands. It does not influence favorably or unfavorably infections of the larynx, bronchi and lungs, as they occurred equally in the two groups. It does not prevent scarlet fever or measles, but may influence the severity of the infection. It seems to lessen the incidence of diphtheria by removing fertile soil for the diphtheria bacillus. It has not influenced the incidence of chorea or rheumatism. It has shown a lessened incidence of heart disease over a period of three years. It has definitely reduced malnutrition in the group operated upon as compared to the group not operated.

Postencephalitic Behavior Disturbances without Physical Signs.—BEVERLY and SHERMAN (*Am. Jour. Dis. Child.*, 1924, **27**, 565) say that a sufficient number of postencephalitic behavior cases have been

studied to enable them to recognize a fairly constant symptomatology. A history of influenza or an undiagnosed condition with diplopia, a permanently developed strabismus, or a protracted period of somnolence is frequently obtained, and should immediately arouse suspicion. The mental and personality changes date from the illness or develop after a period of time even to several years. Personality changes manifested by a change in disposition, inability to sleep at night, violent outbursts of temper, irresponsibility, incorrigibility at school, hindrance in school work, cruelty to animals, lying and the like are the most frequent complaints. The delinquencies are nearly always committed alone and are influenced only slightly by changes in environment. Deterioration of intelligence, poor memory, and poor attention are nearly always reported by teachers and parents. The psychologic examination gives no evidence of mental deterioration. The attention and other mental capacities are normal, except for changes due to the emotional disturbances. The general impression after observing their behavior under examination is that the intelligence is low. The childish mannerisms, impulsive nature of the delinquencies, poor insight into their mental difficulties, the appearance of deterioration, are in marked contrast with the high rating obtained by intelligence tests. This is the most outstanding characteristic. All of these findings are referred to a definite time of onset. In a large percentage of children there is hyperactivity, irritability, alertness and marked emotional instability, the emotional tone varying from extreme anger to a cordial attitude in a few seconds. In a much smaller percentage of cases there was marked indifference, lack of initiative and sluggish body activity. Often there is a paroxysmal polypnea with the emotional outbreaks. In 1 case there was mental difficulty manifested by extremely slow comprehension. In another case there was marked weakness of the extremities which was the initial complaint.

A Comparison of the Metabolism of Some Mineral Constituents of Cow's Milk and of Breast Milk in the Same Infant.—Wang and Davis (*Am. Jour. Dis. Child.*, 1924, **27**, 560) studied chlorid metabolism. They found that change of diet from breast milk to cow's milk was invariably followed by an increase in the chlorid excretion in both feces and urine and *vice versa*. The increase is due, at least in part, to the increased chlorid intake in cow's milk. The average intake with cow's milk was 1.4817 gm. per twenty-four hours and with breast milk 0.4441 gm. The average excretion in feces was 0.1128 gm. and 0.0576 gm. respectively, and in urine 1.0988 gm. and 0.3298 gm. The utilization of chlorid runs parallel to the urinary chlorid; with breast milk it is 0.3847 gm. per twenty-four hours and with cow's milk, 1.3691 gm. There is no marked difference in percentage utilization of chlorid intake between the two milks. For breast milk the average utilization was 87.4 per cent as against 92.2 per cent for cow's milk. There was great variation in chlorid retention in different individuals. The average retention for breast milk was 0.0886 gm. per twenty-four hours, or 19.2 per cent, and for cow's milk 0.2710 gm. or 18.9 per cent. As age increased there was a decrease in the actual retention of chlorid with cow's milk, but no such relation existed with breast milk. There was no definite relation between age and percentage retention. Change of milk had no

effect on the chlorid content of the blood. On a diet of breast milk the average blood chlorid was 627.7 mg. per hundred cc of blood plasma, and on cow's milk it was 618.1 mg.

The Effect of Fluid upon the Temperature and Blood Concentration in the New-born with Fever.—BAKWIN, MORRIS and SOUTHWORTH (*Am. Jour. Dis. Child.*, 1924, **27**, 578) emphasize two points of interest. The striking parallelism between the effect of fluid on the blood concentration and on the temperature in the new-born with fever offers strong evidence in favor of the view that this particular type of fever is due to dehydration. The great efficacy of the oral over the subcutaneous or intraperitoneal routes in reducing the concentration of the blood and lowering the temperature in the new-born with dehydration is of great interest. When the fluid is given by mouth it enters the blood promptly as is indicated by a fall in the serum protein concentration and in the red cell count. When the fluid is given hypodermically or intraperitoneally the fall in blood concentration is neither so marked nor so prompt as in gavage. Apparently a process exists whereby fluid given by mouth is promptly absorbed into the blood and tissues. Fluid given into the subcutaneous tissues or the peritoneal cavity enters the blood much more slowly and to a much less extent. Similar results were obtained in older infants dehydrated as a result of severe diarrhea.

The Clinical Value of the Routine Examination of Blood Smears in the Diagnosis of Pertussis.—HEIMAN (*Arch. Ped.*, 1924, **41**, 385) studied 300 cases of pertussis and suspected pertussis. He based his tests on a relative lymphocytosis. One hundred white cells, stained with Jenner's dye, were counted and for practical purposes a simple division, including only polymorphonuclear cells and lymphocytes, was made. The eosinophilic leukocytes were included in the polymorphonuclear and the transitional cells in the lymphocytes. Small and large lymphocytes were grouped together. The entire procedure takes but a few minutes. The first group included those cases that were unquestionably pertussis. The majority had a history of exposure to the infection. They all had the characteristic persistent spasmodic cough with frequent vomiting. In 75 per cent of the cases a distinct whoop was present. Of this group of 124 cases, 106 or 65.5 per cent showed a very definite lymphocytosis. The ages of this series ranged from three weeks to thirteen years. The second group of cases included those with suspicious coughs which later showed unquestionable symptoms of pertussis. They were all seen within the first two weeks of the infection, about half of them during the first week of the cough. Twenty five cases gave a history of exposure, while 59 did not. In the latter cases it was certainly not possible to venture a diagnosis from the history and physical examination alone. Of this group of 84 cases, 69 or 82 per cent showed a very definite lymphocytosis. In the third group of 57 cases including those with suspicious coughs which subsequently proved not to be pertussis, the patients were seen within about two weeks after the onset of symptoms. In each case the mother was asked to report if the cough became less marked or disappeared. In none of these cases did a whoop develop nor did the cough become progres-

sively worse. In this group are included only those whose subsequent course could be followed. Only 10 or 17 per cent of this group showed a lymphocytosis. The last group of pertussis suspects numbered 35 cases, and this group included those cases whose subsequent course could not be followed carefully enough to allow of any definite conclusions. The impression left by going over the incomplete results are in accord with the results obtained in the other groups. While the routine examination of these 300 patients did not bring forth any positive method of diagnosing pertussis, but the results emphasize the almost constant occurrence of lymphocytosis which should be an aid in the early detection of this infection.

OBSTETRICS

UNDER THE CHARGE OF

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The Pyelitis of Pregnancy.—VAUX (*Am. Jour. of Obstet.*, 1923, **6**, 681) analyzing records of patients suffering from the pyelitis of pregnancy, found that they were generally undernourished, somewhat anemic, and in some a hyperplasia of the thyroid gland was present; but in none was there serious defect or disease. Half of these patients had had their tonsils removed and the remainder showed no evidence of chronic tonsillitis. Their teeth were invariably poor and some had pyorrhea: In 3 cases there was evidence of cardiac lesions with normal compensation and none had serious pulmonary lesions. Some had previously had abdominal operations, and some had lacerations of the genital tract. All had vaginal discharges varying from a moderate thin white discharge to profuse mucopurulent leukorrhea. The Wassermann reaction was negative in all; only one gave a positive Neisserian reaction. Mixed infection of low grade was usually present. The histories showed that the condition began gradually, the patients having no treatment until it became severe enough to disturb the general health. One or both kidneys were usually involved. The writer is inclined to ascribe the occurrence of this complication of pregnancy to the combination of normal anatomical and physiological changes occurring in pregnancy; thus anatomically there is obstruction to the discharge of urine, leading to its accumulation in the pelvis of the kidney. Residual urine is usually present in the bladder during pregnancy. The right kidney was more often involved. The first symptoms of which the patients complained was usually frequency of urination. Anemia usually developed. The normal bladder reflexes varied greatly; in some there was constant tenesmus, while others had little desire to empty the bladder. The colon bacillus was always present, but one case showing streptococci. Cystoscopically hyperemia with a small amount of apparently cloudy urine dribbling into the bladder was found. There was no necrosis of the

bladder wall nor were there areas of hemorrhage, laceration or polypoid growth, nor calculi present. In one instance an abscess at the root of a tooth was present. The blood was usually of the type known as Group 4. There was no mortality among these patients and in but 1 case was labor induced at the seventh month. The treatment consisted essentially of rest in bed with milk and water diet. The Fowler or semi-Fowler position, the knee-chest posture, were used three times a day for five minutes, and patients were requested not to sleep habitually on the right side. Free catharsis was useful. Vaccination and intravenous medication were useless, annoying, and caused excessive reaction. Flushing the pelvis of the kidney was irritating and useless, while in severe cases with vomiting and general weakness, 5 per cent soda bicarbonate solution, one pint every six hours given in the bowel, was of definite value. In serious cases a subcutaneous injection of 500 cc of normal salt solution was valuable. Potassium citrate in large doses by mouth gave some relief of symptoms, while urotropin was without result. Opiates were used as needed. The removal of foci of infection was found to be useful and hot applications over the kidneys gave the patient comfort. A liquid diet at first, followed by an abundant and highly nutritious one was essential. The usual course of the complication was from seven to seventeen days before the temperature and pulse became normal and tenderness disappeared. Pus and bacilli were present, however, in the urine of these cases throughout the remaining months of pregnancy and sometimes after delivery. In the one case in which pregnancy was interrupted the patient grew rapidly better after the interruption. As a rule it is much better to make no cystoscopic examinations, to omit catheterization of ureters, to relieve the bladder of residual urine and when cystitis is present to irrigate the bladder with a mild solution. The writer believes that the real infection is primarily of hemotogenic origin, although the blood stream culture is invariably negative because of the high germicidal qualities of the maternal blood. Stress is laid upon obstruction in the lower urinary tract in promoting infection of the kidney and its pelves.

A Difficult Diagnosis During Pregnancy.—CLIFFORD (*Brit. Med. Jour.*, 1923, **2**, 1045) describes the case of a married woman apparently pregnant in whom the movements of the child had been active until two days before admission. She was apparently at full term, the fetal elements were very plainly to be felt, the head was high up and in the right occipo-posterior position, heart sounds and movements were absent. The cervix was protruding from the vagina and no presenting parts could be felt. A Roentgen-ray examination gave no information. There was slight rise of temperature and the cervix was cleansed, replaced and a ring pessary was inserted. As labor did not develop, the patient asked to leave the hospital. Three weeks later she returned with the same condition but a slightly higher temperature. An effort was made to induce labor by inserting bougies, but they could be passed but 3½ inches although two attempts were made. The temperature was 102° F. and the pulse 120. A stock residual vaccination was administered and ten days later the abdomen was opened when a full term macerated fetus was found in a sac with the placenta almost entirely attached to the outer abdominal wall. The placenta was separated without bleeding, the membranes were not removed. The cavity was

drained and irrigated by the Carrel-Dakin method for three weeks. In six weeks nothing but a small sinus remained. On closely questioning the patient it was found that she had previously had severe abdominal pain with vomiting followed for five days by some vaginal hemorrhage. A surgeon had examined the patient who diagnosed appendicitis, but apparently operation was refused. The reviewer recently had occasion to study the case of a young woman, married five months, with a history of considerable emaciation, the last menstrual period being irregular and repeated with vague pelvic discomfort. On examination on the left side was an elastic mass which could not be differentiated from the uterus. The breasts were poorly developed. There was temperature of 102° F., the urine was normal. The emaciation of the patient and the history of cough suggested tuberculous infection; and the possibility of ectopic gestation was also considered. A Roentgen-ray examination of the abdomen and pelvis gave no information whatever. Physical examination of the chest gave roughened breathing without rales and no expectoration. There was a leukocyte count of 20,800. The patient had a moderate primary anemia. On section the pelvis was roofed over by chronic peritonitis with adhesions. There was peritonitis along the cecum. With considerable difficulty a mass on the left side was dissected with the fingers and from the floor of the pelvis a cystic body the size of a lemon was shelled out, whose wall contained some pus and whose cavity on opening revealed a dark chocolate fluid. The tube and ovary could not be distinctly recognized on the left side. On the right the ovary was bound down with a mass of adhesions, the identity of the tube had been lost in a chronic mass of exudate with numerous small cysts. The appendix could not be found. Drainage was introduced, stimulants given, but the patient became rapidly toxic, dying in forty-eight hours. At autopsy peritonitis was present, but from gross examination of the specimen removed and the body of the patient a positive diagnosis of the pelvic condition could not be made. There was no evidence of tuberculous infection in any part of the body. The appendix was high up behind the cecum and was subperitoneal. The pus was odorless and until a complete microscopic study of the tissues had been made, the exact diagnosis remained unknown. It was fair to infer from the general emaciation, the cystic character of the diseased tissues, the marked pelvic and cecal peritonitis, that a chronic infection or possibly the beginning of malignant degeneration of the ovaries was present. In many respects the history of this patient was typical of an early tubal gestation on the left side. Microscopic study of the tissues removed showed chronic tuberculosis of both Fallopian tubes.

Contraception.—In the *Journal of the American Medical Association* (1923, **81**, 303) is an editorial based upon an article in the *Practitioner*, which devotes its entire July issue to the presentation of views of ten well-known British physicians on the subject of contraception. Economic and sociologic questions were discussed at the 5th International Conference held in London in July, 1922. At this time the opinion of those interested in the subject in Europe was freely expressed. In view of economic conditions in Europe at the present time, the subject is of especial importance because of the lack of population in some countries and the relative excess in others and the question of employment. In the British Isles the territory is limited by natural boundaries, and these

problems have become intensified during and since the World War. The physicians whose views are published discussed the physiologic and pathologic aspects of contraceptive methods, now generally known and available to the informed. Of the ten medical authorities, nine were in virtual agreement as to what constitutes the ideal method of contraception. The problem appeared to be to decide how the available information was to be brought to the attention of those most needing it and how such persons are to be encouraged to avail themselves of it. Under present conditions the tendency is to reach a new point of view upon this subject, with the presenting of reliable information, provided this can be done in the proper manner. Efforts have been made in the United States to publish such propaganda and such efforts have, in numerous cases, been resisted by the authorities. The obstetrical profession in the United States is not prepared at present to endorse this method, for many of the meetings held by those who are active in it, did not convince physicians who attended these meetings, that the information given was reliable or that the general effect upon the public would be good. Those persons who wish to avoid the responsibility of rearing children among the intelligent, well-to-do class are usually successful in so doing; they need no further advice upon the subject, many of them deliberately shirk their duty to the nation. Cases which appeal most to the obstetric profession for limitation of conception are seen in families of artisans or other workers, many of them professional persons of small and fixed incomes, where the size of the family has reached a point that the utmost exertions of the parents can provide for a decent life only, with few comforts and no luxuries. Among the poor many of these mothers become tuberculous or contract diseased conditions of the heart from infection and overstrain in caring for their children. The problem for the physician is to save the lives and health of these women and restore them with strength sufficient to care for their children. In the experience of the reviewer, obstetric surgery is the only reliable agency which can help such individuals. We now have successful methods of analgesia and local anesthesia so that we can terminate a threatening pregnancy and perform sterilization, leaving the ovaries and the uterus to continue the function of menstruation. The reviewer has a number of these cases in his records in whom the result of such operation has been largely satisfactory. He believes this method of birth control to be efficient, decent and justifiable in the case of multiparous women when further pregnancy threatens the health and life of the mother.

Severe Disturbance of the Heart Produced by Pregnancy.—SCHUBERT (*Zeitsch. für Geburtsh. und Gynäkol.*, 1923, **85**, 593) describes the case of a patient, aged thirty-one years, who during her fourth pregnancy had great disturbance in the action of the heart with pain in the chest, dyspnea and prostration. In a subsequent pregnancy she became so much worse that at the third month she sought hospital care with the possible termination of pregnancy. On examination, an old mitral insufficiency of moderate degree was found, but the striking element in the case was the extreme irregularity in the action of the heart. The pulse-rate with the patient at absolute rest in bed varied from 170 to 80. The electrocardiogram showed extrasystoles, but the underlying cause of the irregularity was not elicited. Treatment was unavailing, the

patient became worse although for three weeks every effort was made to improve her condition and avoid the interruption of pregnancy. Finally under ether anesthesia, supravaginal hysterectomy was performed. The patient was discharged fifteen days after the operation with a pulse somewhat too frequent and irregular, but three weeks later her pulse was 70 and the electrocardiogram showed no abnormality. The Roentgen-ray picture of the heart was also normal. Whether this condition was the result of toxemia is an unanswered question. In the observation of the reviewer within a few months a patient, about eight months pregnant was sent into the Maternity Department of the Jefferson Hospital, suffering greatly from dyspnea and inability to lie down and sleep. Mitral stenosis with decomposition was diagnosed by medical consultants. The urine was practically normal, blood-pressure was low and the action of the heart so irregular and disordered that the sounds of the various valves could not be differentiated and a diagnosis of auricular fibrillation was made. Under rest in bed, digitalis and careful feeding and regular emptying of the bowels, the patient's physical condition very much improved. She then became disturbed mentally, refused treatment and became very difficult to control, she was transferred to the psychopathic ward of the Philadelphia General Hospital. She became more quiet and was then sent to the maternity department where she gave birth, without warning, to a living, slightly premature child. Labor was followed by attacks of cardiac syncope which were at first alarming; from this however, she rallied and insisted upon going to her home. Her mental condition never entirely cleared and she was practically uncontrollable. The ordinary tests for the toxemia of gestation failed in her case. There was no hemorrhage at labor and the condition of the heart seemed hopeless. Later the patient was admitted to the Medical Wards of the Hospital suffering from a severe pneumonia but this was weeks after the birth of her child and the pneumonia could not have been present while she was under obstetric observation. So far as medical tests were concerned there was no adequate explanation of her condition.

The Measurement of the Pelvis by the Roentgen Rays.—W. R. MACKENZIE (*Jour. of Obstet., British Empire*, 1923, **30**, 556) contributes an interesting and well-illustrated paper upon this subject. He gives various measurements and includes two plates of pregnant patients one showing the fetal head about to engage five hours before the commencement of labor, the other showing a compression of the cranium in attempted labor with contracted pelvis. In order to procure accurate results he calls attention to the necessity of a standard plate for pelvic measurements. When such an investigation is made the patient must be radiographed in the same position as the standard plate with the same point of focus, the roentgen-ray tube at the same angle to and the same distance from the sensitive plate. If these precautions are taken the various pelvic diameters can be worked out and the variety of pelvic contraction, if present, can be shown. This is the least tiring and uncomfortable method for the patient, of measuring the pelvis. By the coöperation of the Roentgenologist and the obstetrician both maternal and fetal life can be conserved. In none of his cases thus examined during pregnancy was intrauterine death produced, nor was there any physical or mental maldevelopment in the newborn child.

GYNECOLOGY

UNDER THE CHARGE OF

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Operative Treatment of Uterine Prolapse. In the Mayo Clinic, according to MASSON (*Jour. Iowa State Med. Soc.*, 1924, **14**, 174), cases of uterine prolapse which require operative treatment are divided into three main groups: (1) Those in which it is expedient to preserve the function of the pelvic organs; (2) those in which it is important to preserve the pelvic organs, but in which there are no contraindications to producing a sterile state; (3) those in which the patients are near or past the menopause, and there is no contraindication to removal of the uterus. In treating patients during the child-bearing period an attempt should be made to restore as nearly as possible the normal relations. Repair of lacerations is, therefore, preferable to amputation, and shortening of ligaments to making fixations, or radical changes in the anatomical relations. It is important to treat these patients as early as possible, not only to relieve the pain and discomfort, but to prevent the necessity of a more radical operation later. If a young woman has a prolapse of the first or second degree, and there is no indication for opening the abdomen, and external shortening of the round ligaments of the Alexander type, repair of the pelvic floor and in certain cases vaginal fixation or plastic operation on the anterior vaginal wall, has been found to be very satisfactory in the Clinic. However, opening the abdomen adds only slight, if any, risk to the operation, and permits the inspection of other abdominal organs, so that, of late a modified Gilliam internal shortening of the round ligaments has been the operation of choice in such cases. In cases of older women, especially if there is a large cystocele, a plastic operation on the uterine ligaments and repair of the pelvic floor will not be sufficient. In most of these long-standing cases it is not the low-lying uterus that causes the discomfort, but the associated cystocele or rectocele, and treatment should be instituted to relieve these conditions. If the cystocele is large, and the body of the uterus still remains in the pelvis, the most satisfactory operation that Masson has found is the interposition operation of the Watkins-Wertheim type. In many instances the cervix is elongated and high amputation is advisable. If the patient has not passed the menopause the Fallopian tubes must be ligated when performing this operation, to prevent further conception which might prove dangerous. As the degree of prolapse increases, the prospect of cure by the regular Watkins technic decreases, and the failures following this operation are in the main due to an unwise selec-

tion of cases. In cases in which the uterine prolapse is the chief cause of complaint, and the cystocele is not marked, fixation of the uterus and perineorrhaphy give very satisfactory results. If there is only a moderate amount of prolapse vaginal fixation of the Mackenrodt-Duhrssen-Winter type or fixation of the fundus to the anterior abdominal wall by any of the well-known methods is advisable, but if the relaxation is marked, and the uterus can be delivered through the abdominal incision the Kocher or Murphy method, or a partial hysterectomy and fixation of the stump, is advisable. In extreme cases total hysterectomy should be performed, and the vault of the vagina fixed to the abdominal wall. In prolapse of the third degree, in which the cervix to the level of the internal os protrudes from the vulva, and the body of the uterus is in the lower pelvic strait, the author believes that the most satisfactory operation is that devised by C. H. Mayo, consisting of a vaginal hysterectomy with lateral apposition of the broad ligaments, with round and uterosacral ligaments included, and stitching these ligaments into the opening in the uteropubic fascia in exactly the same manner as the uterus is used in the Watkins-Wertheim operation. In cases of complete procidentia the uterine ligaments give little or no support, unless the approximation is made high, and in doing this there is considerable danger of injury to the ureters. However, most of the recurrences of cystocele following the Mayo operation are due to failure to appreciate the necessity of firmly fixing the uterine ligaments into the defect in the uteropubic fascia; that is, fixing the approximated ligaments firmly under the bladder, leaving just sufficient space for the urethra to protrude under the pubic arch, and also anchoring them into the entire length of the anterior vaginal wall. In cases of procedentia in elderly women, and in cases of extensive recurrence following any of the recognized types of operations, partial obliteration of the vagina is justifiable, provided the patient understands exactly what it means. In all cases of uterine prolapse if the pelvic floor is lacerated or relaxed repair of the pelvic floor is indicated, no matter what type of operation has been done to support the upper pelvic diaphragm.

Total Versus Subtotal Hysterectomy as Operation of Choice.—For several years there has been quite a bit of discussion among gynecologists as to whether or not a total hysterectomy should always be performed whenever removal of the fundus is indicated. Those in favor of the total operation base their opinion on the fact that occasionally carcinoma develops in the retained cervical stump, and they state that the mortality of the total operation is only very slightly higher than that of the subtotal operation. From a study of the literature, as well as from personal investigation, BLACK (*Texas State Jour. Med.*, 1924, **19**, 664) concludes that total hysterectomy is the operation of choice in all cases of suspected malignancy of the body of the uterus and in badly lacerated or diseased cervices complicating fundal conditions requiring uterine removal. In the treatment of myomata total hysterectomy is the operation of choice only in women approaching or past the menopause or with diseased cervices. In uterine myomata in young women, with apparently normal cervices, especially if the patient has a large adherent fibroid, making a total operation hazardous,

a subtotal hysterectomy is the operation of choice. When an abdominal hysterectomy is indicated, with extensive inflammatory changes surrounding the uterus, or when the pelvic diaphragm is fixed and there is a diseased cervix, a subtotal hysterectomy with amputation of the cervix is the operation of choice. Vaginal hysterectomy is the operation of choice in cases of procidentia or in the fat or aged with vaginal relaxation or some prolapse. Vaginal hysterectomy is attended by a very small mortality rate in properly selected cases. Although it is commonly stated that there is very little difference in the mortality between subtotal and total hysterectomy, this fact only applies when the operations are done by experts. In general, the mortality in the hands of the average surgeon is 9.44 per cent for the complete operation against 5.29 per cent for the subtotal operation. Therefore Black correctly advises that the subtotal hysterectomy should always be the operation of choice in the hands of most men, and this fact should be taught in our medical schools.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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A Scarlet Fever Antitoxin.—Although curative serums for streptococcus infections have been made by various investigators, the large dosages required would seem to indicate that any curative antibodies contained in these serums are present in low concentration. With the idea of producing a scarlet fever antitoxin, DICK and DICK (*Jour. Am. Med. Assn.*, 1924, **82**, 12) immunized a horse by subcutaneous injections of sterile filtrate from broth cultures of the strains of streptococci that had produced experimental scarlet fever. After increasing doses of toxin, up to 250 cc, had been given, it was found that 10 cc of the serum contained antitoxin sufficient to neutralize twenty times the amount of toxin that produced nausea, vomiting, general malaise, fever of from 100° to 101° F. and a definite scarlatinal rash in susceptible adults. Concentration did not destroy the antitoxin. The authors feel that "The therapeutic value of the antitoxin can be determined only when the results of its use in a large series of carefully controlled cases are available."

Results Obtained with the Dick Test in Normal Individuals and in Acute and Convalescent Cases of Scarlet Fever.—Having conducted studies with the Dick test among normal individuals along lines similar to those carried out with the Schick test, ZINGHER (*Proc. Soc. Exper. Biol. and Med.*, 1924, **21**, 293) found that the susceptibility by age

groups from birth to adult life corresponded closely to the percentage susceptibility to diphtheria, as shown by the Schick test. The reactions in the mother and offspring during the first six months of life were similar. The blood serum of a person giving a "negative" or a "pseudo" Dick reaction caused blanching of the rash and neutralized the test toxin, while that of a "positive, or a combined," reaction caused no blanching of the rash and did not neutralize the test toxin. The Dick test was positive, as a rule, during the first two days of scarlet fever, but became less positive toward the end of seven days and negative toward the end of ten to fifteen days, when the antitoxic properties began to appear in the patient's serum. The neutralization of the test toxin was found to be a more delicate index of the presence of antibodies in a serum than its property to cause blanching of a scarlet-fever rash—the Schultz-Charlton test. Four reactions were recognized with the Dick test—all of which correspond closely to the similar four reactions noted with the Schick test. These reactions are a positive, a negative, a pseudo and a combined. The positive reaction closely resembled at the end of twenty-four hours a positive Schick test which had reached its maximum on the third or fourth day. It appeared within six to twelve hours, reaching its height at the end of twenty-four hours and faded fairly rapidly. A good positive reaction was followed by pigmentation, with very slight or no scaling. The pseudo reactions were found to be due to the autolyzed bacterial substance of the streptococcus and other proteins in the test fluid. They were not specific, and could be separated from the positive reactions by a control test, using toxin neutralized with an equal amount of 50 per cent convalescent serum or of normal serum from negative Dick reactors. In a pseudo reaction the same appearance obtained with both the toxin and the control. It was most frequently encountered in old children, adults, and in some who gave a previous history of scarlet fever. The combined reaction showed a much more pronounced redness at the site of the Dick test as compared with the control test. The author considers that the positive and combined reactors are probably susceptible; the negative and pseudo reactors are probably immune to scarlet fever. The toxin was destroyed at 100° C. for forty-five minutes in dilutions of 1 to 100, so that in all probability the author will use the heated toxin for purposes of control, as in the Schick test. The positive reaction noted in all early cases of scarlet fever and the subsequent negative or pseudo reaction during convalescence in nearly all these patients would indicate that the different agglutinative strains of hemolytic streptococci found in the throats of scarlet-fever patients produce the same antitoxic antibodies. The Dick test was found very valuable for diagnostic purposes, as a positive reaction obtained during the first day or two of a suspicious scarlet-like rash and again two weeks or more after the fading of the rash indicated that the patient did not have scarlet fever. The author considers the Dick test of great value, with an increasing field of application in the selection of susceptible individuals for passive and active immunization, for passive immunization with convalescent serum from human beings or antitoxic serum from animals and for active immunization with increasing doses of the toxin itself. For active immunization the author is using 25, 50, 100 and 200 skin test doses, the injections being given intramuscularly about a week apart.

Further Studies on the Potency of Botulinus Toxin.—By titrating botulinus toxin from day to day, BRONFENBRENNER (*Proc. Soc. Exper. Biol. and Med.*, 1924, **21**, 318) observed that determinations of the potency of dilutions of toxin in physiological salt solution frequently gave inconsistent results, due to the fact that NaCl, as well as many other salts of monovalent and polyvalent metals had a direct deteriorating effect upon the toxin. This effect was more marked the higher the dilution of the toxin, the longer the exposure and the higher the concentration of the salts. If the toxin were diluted in distilled water the results of titration were more regular. In the presence of low concentration of salts addition of serum or broth seemed to protect the toxin from deterioration. Toxin diluted directly in normal horse serum or in ordinary broth had an increased potency. In view of this, the author points out that it is important to determine carefully the type of toxin involved before administering antitoxin, as experiments have shown that animals receiving heterologous antitoxin (Type B), together with botulinus toxin (Type A), died more promptly than the controls receiving toxin alone.

Culture Filtrates of Hemolytic Streptococci from Scarlet Fever: Intracutaneous Reactions in Test Animals.—Employing the Dick toxic filtrate obtained from cultures of hemolytic streptococci from scarlet fever, WILLIAMS, HUSSEY and BANZHAF (*Proc. Soc. Exper. Biol. and Med.*, 1924, **21**, 291) found that the intracutaneous injection of these filtrates in young depilated rabbits gave a very clear-cut reaction and that the filtrates were neutralized by serum from convalescent scarlet-fever patients. The reaction in guinea-pigs was not as clear cut as in the rabbits. The strongest and most lasting reaction in rabbits was obtained in the filtrates from a forty-eight hour growth. While the convalescent scarlet-fever serum seemed to neutralize the filtrates of the growth of the hemolytic streptococci from scarlet fever, as shown by the intracutaneous reaction in rabbits, it did not neutralize toxic filtrates obtained in the same way from Staphylococcus pyogenes or from Escherichia coli. Neither did it neutralize a toxic filtrate obtained from a hemolytic streptococcus from endocarditis, while it did neutralize one isolated from a wound infection, which had been included by absorption of agglutinins in our agglutinative group of hemolytic streptococci obtained from scarlet fever.

The Pathogenesis of Rheumatic Fever.—"It is surprising that in spite of the great advance in the knowledge of the causation of the most common infectious diseases, we still must recognize our uncertainty of the etiological agent in this infection (rheumatic fever). Certain contributing environmental factors have been suggested, and nonhemolytic streptococci have been claimed by several authors to be the causative microörganisms, but the failure to recover these streptococci from a majority of patients and the fact that the classical disease presented by man has not been reproduced by inoculating them into lower animals have caused most students to hesitate before considering the question settled." Consequently, to obtain a better understanding of rheumatic fever, SWIFT (*Jour. Exper. Med.*, 1924, **39**, 497) has correlated the clinical findings of the patient with the examination

of the various tissues that can be obtained from the subject during life and after death. The gross clinical manifestations of rheumatic arthritis are pain, tenderness, swelling, redness and local heat diffusely distributed about the joint. The synovial fluid contains many exudative cells, mostly polymorphonuclear leukocytes. "Remarkable features to the acute arthritis are: (1) The tendency for the inflammation to migrate—to jump—from one joint to another without any apparent involvement of the intervening tissues; (2) the failure of the process to go on to suppuration; (3) the rapid disappearance of the symptoms and signs of inflammation after the patient has taken such antipyretic drugs as certain derivatives of salicylic acid or phenylcinchoninic acid." In fatal cases the most striking gross feature found at autopsy is the appearance of rows of small bead-like excrescences along the free margins of the heart valves. These verrucæ are made up of coagulated elements derived from the circulating blood. Older verrucæ show a definite tendency to heal, becoming covered with endothelium and invaded by organizing connective tissue. But even in the young lesions a distinct proliferative inflammation occurs in the substance of the heart valve. Although it is a moot point whether the destruction of the endothelium is primary or subsequent to an injury to the underlying tissue, it is not difficult to conceive of the primary injury of the valves occurring in their substance rather than on the surface—in which event it would be better to consider rheumatic disease of these structures as a *valvulitis* rather than a simple *endocarditis*. "The most generally recognized specific histological lesion of rheumatic fever is the so-called Aschoff body, which is a submiliary nodule located in the myocardium, usually in close relationship with the small bloodvessels." There is practically always a small central area of necrosis surrounded by peculiar cells, having vesicular nuclei and a cytoplasm that takes a granular red color when stained with methyl-green pyronine; usually many cells are present with multiple nuclei, forming a particular type of giant cell, different from that seen in tuberculosis. At times the bloodvessel lumina may be partially or completely closed by thrombi. The bloodvessels may also be constricted by pressure of Aschoff bodies or by an endarteritis, with swelling and proliferation of the endothelium, as seen in the smaller branches of the coronary arteries. The fibroid nodules in the subcutaneous tissue of children have a histological picture similar to that of the Aschoff body. They occur in the deep fascia over bony prominences and tendon sheaths and tendons. Not being in close opposition to nerves, they are usually painless. The joint lesions consist of focal lesions in the synovia, focal necrosis of the capsule, thrombosis of the smaller arteries and endothelial and perivascular reactions comparable with changes found in the heart and in subcutaneous nodules. The presence of many small nerves in the joint capsule and surrounding ligaments easily explains the great pain in rheumatic arthritis. In chorea minor, thrombi, endothelial proliferation and perivascular collections of round cells, together with small focal changes in the nervous tissue contiguous to these vessel lesions have been described. In summarizing the author says "It is evident that there are two distinct types of response on the part of the body to the infectious agent of rheumatic fever, viz, proliferative and exudative. The perivascular proliferative type of lesion, resembling an infectious granuloma, explains

the subacute and chronic character of the clinical symptoms in many patients with this disease. Marked exudation of serum into the periarticular tissues and of serum and cells into the joint cavities are concomitants of the acute arthritis occurring with high fever and general intoxications; these acute exudations disappear following the administration of certain drugs. But their disappearance does not mean necessarily that all lesions of the proliferative type have resolved. In fact, we know that these last-mentioned lesions, when present in the subcutaneous tissues, often continue for months; and from analogy we may conclude that they have a similar persistent character in other tissues of the body invaded by the causative agent of rheumatic fever."

HYGIENE AND PUBLIC HEALTH

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Syphilis as a Factor in the Etiology of Mental Deficiency.—Weiss and Izgur (*Jour. Am. Med. Assn.*, 1924, **82**, 12) state that it has become increasingly evident to them not only that syphilis is uncommon in mental defectives, but also that it is less common than in the general population, and is comparable in frequency only with congenital syphilis at any lying-in or child-caring institution. Their studies have led them to question whether there is any etiological relationship whatsoever between syphilis and mental deficiency. If syphilis is a cause of mental deficiency it should occur far more frequently in mentally deficient than in mentally normal children; the evidence adduced in their study controverts such an assumption. The feeling has grown more and more that there is no such abnormal mental state as "syphilitic amentia." It seems more than probable that syphilis is an incidental finding in mental defectives; if it bears any relationship to abnormal mental states in children it is recognizable as frank juvenile general paralysis or tabes. These conditions are not common; they are not, strictly speaking, amentias, but dementias, and they usually are not, or at least should not be, confused with primary amentia.

Influence of Lack of Vitamin C on Resistance of the Guinea-pig of Bacterial Infection, on Production of Specific Agglutinins and on Opsonic Activity.—Werkman, Nelson and Fulmer (*Jour. Infect. Dis.*, 1924, **34**, 447) state that the significance of the diet in maintaining a normal resistance to infection has lately assumed increasing importance.

In both human and veterinary pathology a lowered resistance has been shown to result when certain defective dietaries are employed. The vitamins, A and B particularly, have received considerable attention, although the significance of vitamin C has up to the present time remained more or less obscure. The authors find from their studies that guinea-pigs suffering from the lack of vitamin C experience a definite and determinable, though not marked, break in their resistance to infection by the pneumococcus and Bacillus anthracis. The reduced body temperature is of primary significance in accounting for the reduced resistance to infection. Guinea-pigs lacking vitamin C reveal no differences in their ability to produce specific agglutinins for the typhoid bacillus from that of healthy animals. Investigation of the phagocytic activities in guinea-pigs lacking vitamin C revealed no injury to the phagocytic mechanism as the result of vitamin-C deprivation.

Revived Activity of the Virus of Poliomyelitis.—FLEXNER and AMOSS (*Jour. Exper. Med.*, 1924, **39**, 191) describe a strain of the virus of poliomyelitis which has passed through several stages of virulence, as tested upon monkeys. The first stage consisted of the adaptation of the original human virus to the monkey. In this process high virulence was readily achieved. The adapted virulent strain of virus was passed regularly through monkeys and maintained its activity for about three years, when diminution became apparent. The loss of power of the virus was such that it may be said to have returned approximately to the level of the original human virus. This change constituted the second stage. The third stage is represented by recovery of the high virulence. This revival occurred, it seems, during the sojourn of the virus in glycerol, and required several years for its consummation. It was first noticed nearly six years after the low level of the second stage became established. The potent virus of the third stage has been found to remain active over a period of at least four years while preserved in glycerol. What constitutes at least a superficial resemblance between the wave-like rises and falls of the incidence of epidemic poliomyelitis and the phenomena of increase and decrease in virulence of the specimen of virus has been alluded to. The two processes differ, however, essentially in respect to the time factor, since the fluctuations of the epidemic wave occupy small, and those of the virulence occupy large, increments of time.

Penetration of Normal Mucous Membranes of the Rabbit by Treponema Pallidum and the Influence of this Mode of Infection upon the Course of the Disease.—BROWN and PEARCE (*Jour. Exper. Med.*, 1924, **34**, 645) carried out experiments with three strains of Treponema pallidum to determine whether infection could be produced by applying an emulsion, rich in spirochetes, to normal mucous membranes of rabbits, and whether an infection produced in this manner differed in any respect from one produced by other methods of inoculation. It was found that a simple instillation of a spirocheta emulsion into the conjunctival sac or the sheath was all that was necessary to obtain an infection. Still, the infection produced in this manner differed from that produced by intracutaneous or testicular inoculations, in that it tended to pursue a mild or asymptomatic course

and frequently without the development of a characteristic chancre. It is pointed out that these experiments may have a bearing on problems pertaining to obscure and atypical cases of human syphilis, as well as the more immediate question of the infectivity of Treponema pallidum.

Notes on the Longevity and Infectivity of Hookworm Larvæ.—ACKERT (*Am. Jour. Hyg.*, 1924, **4**, 222) states that hookworm larvæ (probably Necator americanus) lived eighteen months in a culture of cistern water. The temperatures to which they were exposed varied from 45° to 98° F., with fluctuations between 60° and 85° F. most of the time. Infectivity tests, made with an adaptation of the Goodey method, and with a live rat, showed that these eighteen-months-old larvæ responded to heat stimulation, but indicated that they were no longer infective.

Experimental Human Inoculations with Filtered Nasal Secretions from Acute Coryza.—ROBERTSON and GROVES (*Jour. Infect. Dis.*, 1924, **34**, 400) secured nasal secretions from 11 persons suffering with acute uncomplicated coryza. After being diluted and passed through a Berkefeld filter, these secretions were sprayed onto the nasal mucosa of 100 volunteers. The authors state that their experiments presented no convincing evidence indicative of a filter-passing organism as the exciting factor in acute coryza, and believe the cases recorded as positive to be the result of factors independent of the inoculations. During an attack of coryza definite variations were noted in the bacterial flora of the secretions. During the onset and early stages of the attack there was a marked diminution of the total bacterial flora, with an equally marked predominance of one of the normal habitants—usually Staphylococcus albus. During the purulent stage of the attack a marked increase of all organisms over the normal flora of health was observed, although the predominance of one organism still remained. The later stages of the attack were marked by a gradual return to the normal flora of health.

Studies on the Relation between Tumor Susceptibility and Heredity.—LYNCH (*Jour. Exper. Med.*, 1924, **39**, 481) presents some of the results obtained from crossing mice from tumor strains with males from other sources. The comparison of the tumor incidence in the inbred and backcross daughters, though the numbers given are small, supports the theory that the tendency to develop neoplasms is hereditary and the frequency with which tumors appear in the first filial generation of such crosses, indicates that the character is dominant. Additional experiments involving larger numbers are in progress.

Is the Prophylactic Use of Diphtheria Antitoxin Justified? DOULL and SANDIDGE (*U. S. Pub. Health Repts.*, 1924, **39**, 283) state that in Baltimore, according to the records of 508 consecutive cases of diphtheria, 10 per cent of the family contacts of ten years and under who were not given prophylactic antitoxin subsequently developed diphtheria, mostly within thirty days. Of the children of the same age group who were given prophylactic antitoxin only 1.2 per cent were

attacked. This experience is in agreement with the experience of other writers with regard to the low secondary attack rates among immunized children and the very much higher rates among children not so treated. At a case fatality rate of 2 per cent the risk of death from diphtheria undergone by unprotected children over that of children given prophylactic antitoxin is, for children of ten years and under, in Baltimore, 1 death to 568 family contacts. The best statistical record of deaths from antitoxin shows 1 death among approximately 75,000 persons injected. When, for any special reason, it is considered inadvisable to administer antitoxin as a prophylactic, the child should be guarded from infection by being removed from the infected home. On removal, such a child should be given the advantage of medical supervision and modern diagnostic methods. The evidence presented emphasizes especially the question of young contacts. It is realized that adults and older children may be subjected to daily examination, and possibly Schick tested. It is probable, indeed that in time this policy might be extended to all children of school age. Young children, however, constitute a special problem because of difficulties of examination and of diagnosis and because of much greater liability to attack. Among these children the use of prophylactic antitoxin is clearly not only justified but demanded.

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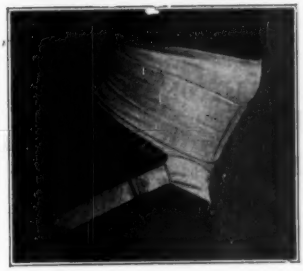

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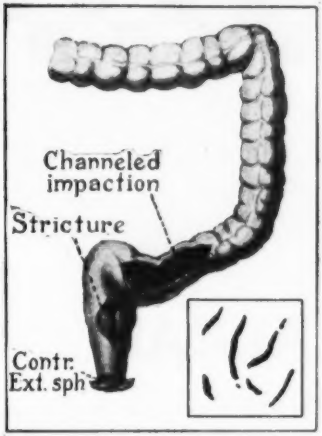
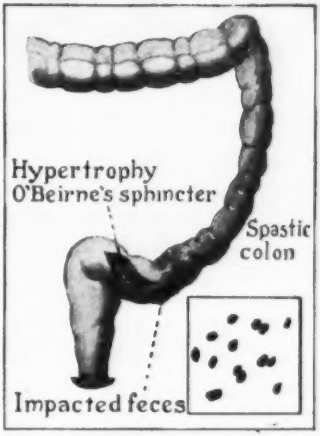


Penciled Stool—In spastic bowel, stenosis, channeled fecal impaction and contracted external sphincter.



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